CARDIAC ISCHAEMIA*

BY

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It is with humility that one approaches a topic of which others have far greater experience but my reason for discussing cardiac ischaemia is that I have been so struck recently by its frequency. In my own practice in the last two years I have encountered no less than 318 cases and the annual toll from this disease in 1957 in England and Wales was over 76,000.

HISTORY

It was Galen who named and described the coronary arteries, but William Harvey who appreciated their function. In 1649 he described a man "who did often complain of an oppression in his breast" and "at last opprest in a signal paroxism, he dyed"; the post-mortem examination showed aortic stenosis and a ruptured left ventricle presumably due to infarction. Much of the pioneer work on cardiac ischaemia has been done by Englishmen, such as William Heberden who in 1768 described "angina pectoris" and Caleb Parry of Bath, Edward Jenner of Berkeley and John Hunter of London who related the symptoms to narrowing of the coronary arteries. Jenner in describing the post mortem of a patient who died in Dursley in 1772 writes "My knife struck something so hard and gritty as to notch it. I well remember looking up at the ceiling, which was old and crumbling, conceiving that some plaster had fallen down. But on further scrutiny the real cause appeared: the coronaries were become bony canals". Parry belonged to a select medical society of five which included Jenner. In a meeting at Rodborough in 1788, he described "syncope anginosa" and related the symptoms to the morbid anatomy thus: "The rigidity of the coronary arteries may act proportionably to the extent of the ossification, as a mechanical impediment to the free motion of the heart, and though a quantity of blood may circulate through these arteries, sufficient to nourish the heart, as appears, in some instances from the size and firmness of that organ, yet there may probably be less than what is requisite for prompt and vigorous action".

FREQUENCY

In 1908, only 929 deaths were certified as due to angina whereas in 1957 there were 76,324 deaths attributed to coronary heart disease. This figure would be even higher if we included the 50,000 people on whose death certificates "myocarditis" or "myocardial degeneration" was written as the cause of death. Some of this enormous increase must be due to more accurate clinical diagnosis with the increased use of the electro-cardiogram following the pioneer work of Eindhoven, Pardee (1920), and Parkinson and Bedford (1928). Other causes are an ageing population and changing of fashion in diagnosis. But there is overwhelming evidence of a very real increase in mortality from coronary artery disease. The death rate from it has doubled since 1947, and nearly 15 per cent of all deaths are now due to it. Coronary artery disease kills nearly as many people each year as cancer in all its forms and sites. Yet I wonder how many mites are spent on research on this disease compared with the gold coffers of the cancer research fund.

* Based on an address to the Bristol Medico-chirurgical Society.

The ratio of mortality in men to that in women varies from 1·4 in Japan to 4·4 in Finland: in the U.K. it is 1·68. Occupation seems to affect mortality: the standardized mortality rate in U.K. is very high among physicians and surgeons (368), barristers and solicitors (227), employers and managers (190) compared with coalminers (40) and agricultural labourers (32). This can be interpreted in several ways: it may reflect the selection for the professions of the most progressive and restless members of the community, or the burden of responsibility which they carry, or a lack of physical exercise or an increased consumption of tobacco and animal fat! Nevertheless, it is a sobering thought that the cause of death of the professional and managerial sections of our community—readers of *The Times*—will in more than a third be coronary artery disease. However, the notion that agricultural workers are less prone to coronary disease may be wrong—Kennedy (1957) found that 24 per cent of his admissions with this disease in Dumfries were farm workers, a proportion corresponding to the population served. It would seem that they have a better prognosis.

Brown and others in Birmingham (1957) showed that the frequency of symptoms from coronary artery disease is higher in sedentary than manual workers. There were also more myocardial infarcts in the professional compared with the unskilled occupations though the prevalence of angina was higher in the manual worker. It is this curious dissociation of cardiac infarcts from angina that has always intrigued me; ischaemic heart disease is not a simple function of coronary artery disease. Jamaican negroes for instance have coronary atheroma as frequently as the white population of the Southern U.S.A., but only rarely suffer from ischaemic heart disease, (Robertson, 1959). Further evidence on this point comes from Morris and Crawford (1958) when reporting a national necropsy survey of the disease. They found no variation among different occupations in the frequency of coronary atheroma or stenosis; ischaemic myocardial fibrosis and coronary occlusions were however, more common in those with light occupations compared with heavy ones, and appeared at an earlier age. There is however one criticism of this work, that the occupations referred to are always the last stated ones—and a man with coronary disease may well change to a lighter job late in life. Nevertheless, should we not perhaps think of ischaemic heart disease as a *deficiency disease*—a deficiency of exercise?

Over-indulgence in alcohol does not seem to be an important factor in coronary artery disease. Barmen and French wine workers show a high mortality rate from cerebro-vascular diseases and chronic nephritis, but only a slight increase from coronary artery disease. Cigarette smoking does seem to be associated with a higher mortality from this disease—about double for those who smoke 20 or more daily (Hammond and Horn). But I do not think that this relationship need be one of cause and effect; both habit and disease may be an expression of a man's emotional make-up.

Hereditary factors are undoubtedly important in this disease—the body build, the coronary arteries themselves and the degree to which they anastomose with each other, the metabolism and the nervous balance of the individual.

DIETARY FAT

There are two ways in which an excess of dietary fat may influence the disease, either by accelerating the development of atheroma, or by provoking intravascular thrombosis—though the two may be related if Duguid's work (1946) is accepted . . . Firstly let us consider the development of *atheroma.*

(1) In experimental rabbits, cholesterol deposition on the arterial wall can be directly related to the height and duration of hypercholesterolaemia artificially induced by a diet high in cholesterol. From this evidence it has been argued that in man, in whom atherosclerosis develops spontaneously, control of the serum cholesterol is both desirable, and beneficial in coronary artery disease. I think this deduction is quite unwarranted.

(2) Patients with established coronary disease are said to have a higher mean level of serum cholesterol than normal subjects (Oliver and Boyd, 1956) and to have a greater and longer lipaemia after eating butter (Barritt, 1956) but these may be the effects, or related abnormalities, rather than the cause of the disease.

(3) Patients who have hypercholesterolaemia, such as diabetics and those with rare familial diseases such as Xanthoma tuberosum, succumb to coronary artery disease more frequently than normal people. This may be so, but it is quite a different matter to infer from this that reduction of the blood cholesterol is therefore desirable or beneficial.

(4) It has been shown that the serum cholesterol can be reduced by a change from animal to vegetable fats (Kinsell 1952, Bronte Stewart 1955). At first this effect was thought to be due to essential fatty acids, then to sitosterol, but now the accepted view is that it is due to the unsaturated fatty acid content of the vegetable fats. These fats are only effective when substituted for saturated fats, not when merely used as supplements. In other words it is no use having potatoes fried in sesame oil and corn oil salad dressing in a meal which starts with pâté de foie gras, progresses to roast pork and ends with strawberries and cream and a slice of Stilton! However, it has yet to be shown that reduction of serum cholesterol has any effect on the prognosis of coronary artery disease.

Secondly, does dietary fat have any effect on *blood coagulation*?

(1) In Aberdeen, Fullerton (1953) showed that there is a shortening of the silicone clotting time after a fatty meal, which is greater in convalescent ward patients than in sedentary students. Mersky and Nossel (1957) on the contrary found no effect on blood coagulation of diets differing in their fat content.

(2) In London some workers (McDonald and Edgill (1957)) showed a difference in various clotting factors between patients with ischaemic heart disease and controls. There was however a considerable overlap and no conclusive evidence was obtained that the hypercoagulability was not the effect rather than the cause of the disease. By contrast O'Brien (1958) in Portsmouth found no difference in the blood coagulation of patients with coronary disease compared with controls after a fatty meal. As he says: "There is no support for the hypothesis that postprandial hypercoagulability is responsible for the alleged connection between the fat content of the diet and coronary thrombosis.

(3) Other work has been done by Greig (1956) on fibrinolysins showing that they are increased after exercise and decreased after a fatty meal. But this work has not been confirmed by other workers.

(4) It can thus be seen that there is much conflicting evidence concerning the effects of fat on blood coagulation. It is important to remember the work of Master et al (1939) who showed that the time of onset of coronary thrombosis was evenly distributed throughout the 24 hours, and thus unrelated to the major meals. Also no thrombosis is found in more than one third of all those dying from infarcts.

Dietary habit studies do not help us to decide about the role of fat. Evidence based on the incidence of coronary artery disease in primitive tribes cannot really be accepted as their life expectancy is so much less than in so-called civilized communities, standards of medical diagnosis are far below ours, and racial factors may be important. Indeed where statistics have been collected carefully as for example by Malhotra and Pathania (1958) from the Punjab, they show that coronary artery disease in India is not a rarity—it formed 28·4 per cent of their cardiac patients. This is even more remarkable when we appreciate that most of these patients were on a low fat diet, many were vegetarians and non-smokers! The figures of Professor Keys (1953) of

Minnesota are often quoted to show that nations with a high consumption of fat (such as the U.S.A.) have a high incidence of coronary artery disease compared with Japan where fat consumption is low. But as Yudkin (1957) showed, although the U.S.A., U.K. and Norway had similar fat intakes, their mortality rates from coronary artery disease varied enormously. (See Fig. 1.) A comparison with Fig. 2 shows that there is almost as close a relationship to sugar consumption.

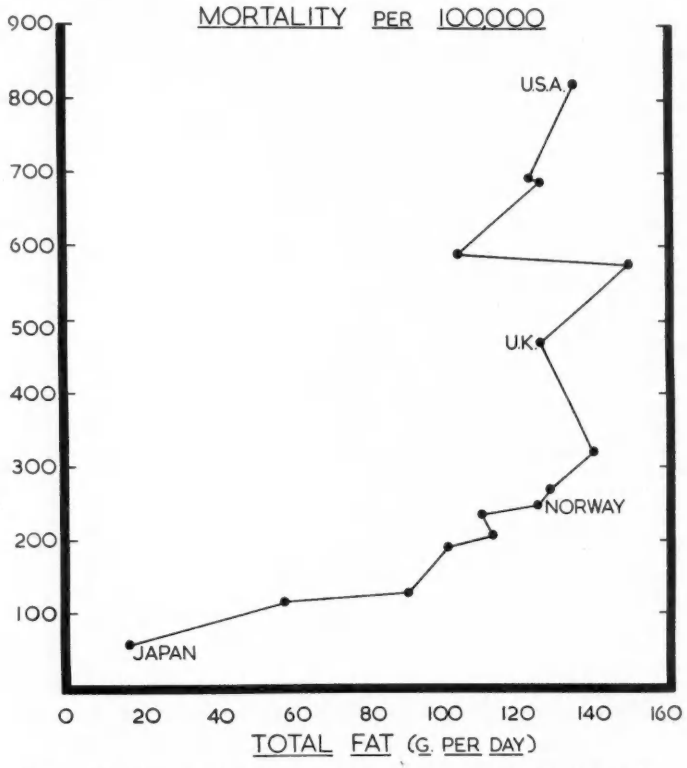

FIG. 1. *Mortality rate from coronary artery disease related to fat consumption. Each dot represents a country: only a few are named for the sake of simplicity.*

Furthermore, there has been no significant change in our dietary habits in the last 20 years to match the relentless increase in coronary mortality. The rising mortality can in fact be related more closely to the number of television licences! (See Figs. 3 and 4).

I am unable to accept a theory which supposes any single or major dietary cause of coronary disease, but I feel that relative over-consumption of food and reduced physical exercise may be contributory causes of the disease. The fall in mortality in Norway during the German occupation may well have been due to reduction of total calorie intake and increased exercise. Until we have further evidence on this subject of diet in coronary disease, I do not feel we are justified in altering our habits. Nor can we

be sure that these unsaturated vegetable fats which some would advocate do no harm; in rats they cause gastric ulcers and even carcinoma. And the mortality rate from gastric carcinoms aged 55–64 in Sweden is two to three times that in the U.S.A.—perhaps due to greater consumption of unsaturated fish oils? In short let us be cautious that we do not jump from our fatty frying pans into the fire of cancerous complications of corn oil.

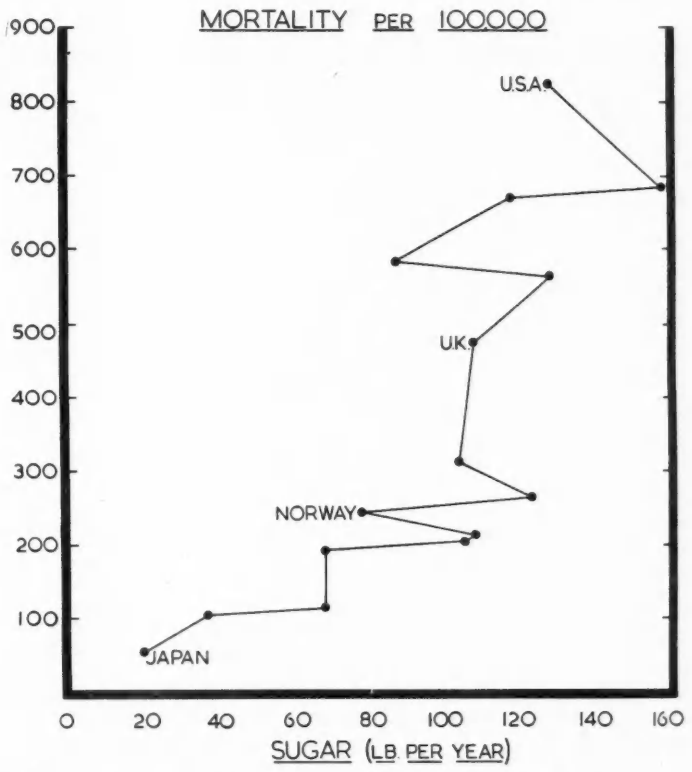

FIG. 2. *Mortality rate from coronary artery disease related to sugar consumption. Note the essential similarity to Fig. 1.*

SYMPTOMS

But enough of statistics. How are we to recognize coronary artery disease in the patients who come before us? In describing the symptoms I make no apology for quoting the masterly description of William Heberden, the man who coined the phrase "angina pectoris".

"They who are afflicted with it are seized while they are walking (more especially if it be uphill), and soon after eating with a painful and most disagreeable sensation in the breast, which seems as if it would extinguish life, if it were to increase or continue, but the moment they stand still, all this uneasiness vanishes.

FIG. 3. *Animal fat consumption (solid dots) in the U.K. during the last forty years related to coronary artery disease mortality (open circles).*

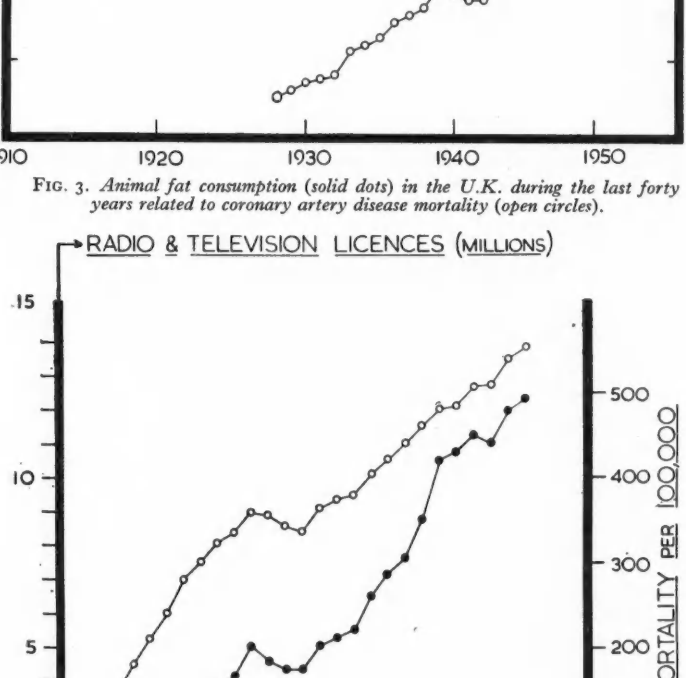

FIG. 4. *Radio and television licences (solid dots) in the U.K. related to coronary artery disease mortality (open circles).*

(*Figs. 1–4 adapted from Yudkin,* Lancet 1957, *by kind permission.*)

"In all other respects, the patients are, at the beginning of this disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different. The pain is sometimes situated at the upper part, sometimes in the middle, sometimes at the bottom of the os sterni, and often more inclined to the left than to the right side. It likewise very frequently extends from the breast to the middle of the left arm. The pulse is, at least sometimes, not disturbed by this pain, as I have had opportunities of observing by feeling the pulse during the paroxysm. Males are most liable to this disease, especially such as have passed their fiftieth year.

"After it has continued a year or more, it will not cease so instantaneously upon standing still: and it will come not only when the persons are walking, but when they are lying down, especially if they lie on the left side, and oblige them to rise up out of their beds. In some inveterate cases it has been brought on by the motions of a horse, or a carriage, or even by swallowing, coughing, going to stool, or speaking; or any disturbance of mind."

Could anyone today really improve on this description? I would only like to emphasize the importance of emotional excitement in producing pain, and one experience which seems to be very provocative is watching a boxing match on television. One patient of mine gets angina when his wife drives the car! I wish also to say how many patients I have seen in recent years in whom the pain of an infarct has been in the left, or occasionally the right mammary line and not substernal. Pain below the costal margin has only been rarely encountered, also pain in the arm alone unless accompanied by chest pain. And remember that in some patients Trinitrin tablets give no relief, presumably because the peripheral vessels relax more than the coronaries.

DIAGNOSIS OF CARDIAC PAIN

The diagnosis of angina rests almost entirely on an accurate history. Physical examination and radiography seldom help, and the E.C.G. helps in only a small proportion. The family doctor who knows the previous personality and family background can best assess whether the symptoms stem from anxiety about the heart or from coronary artery disease. Confusion with *Hiatus Hernia* may occur but symptoms from the latter usually have an association with eating or posture, and it must be remembered that the demonstration of a hernia does not necessarily mean that it is the cause of the symptoms. This remark also applies to *Cervical Spondylosis:* pain from this common condition may pass round to the front of the chest as well as down the arm, but there is usually a history of neck pain and of a wrench of the arm or neck at the onset. Symptoms from a diseased *Gall Bladder* may exist at the same time as those from cardiac ischaemia, and there is interesting experimental evidence that distension of a hepatic duct may cause a reflex fall in coronary blood flow. It can sometimes be a nice clinical problem to decide whether a diseased biliary system is contributing to cardiac symptoms. Gall Bladder pain may be midline, but is seldom felt in the chest, and is not related to effort.

When a diagnosis of cardiac pain has been made, this is not tantamount to saying that coronary atheroma is the only disease process present. *Anaemia* must always be considered and haemoglobin estimation done if there is any doubt. Many patients obtain complete relief when the anaemia is corrected. *Aortic Stenosis* or incompetance may be the cause of cardiac pain, but relief here is most difficult. *Hyperthyroidism* by increasing the work of the heart may cause pain. A patient of mine with acromegaly and hyperthyroidism required 20 trinitrin tablets daily in order to control angina. After treatment with neomercazole and later thyroidectomy she needed none. *Paroxysmal Tachycardias* may cause cardiac ischaemia, and their control by digitalis, quinidine or procaine amide usually brings relief from pain. *Syphilitic Aortitis* is now rare

but it may cause cardiac pain by narrowing of the coronary ostia. Attempts to relieve the pain by anti-syphilitic treatment are usually unrewarding.

Occasionally cardiac pain occurs during *Rheumatic Fever* probably because of coronary arteritis and a youth whom I saw recently had this pain when cycling as the first evidence of carditis.

DIAGNOSIS OF CARDIAC INFARCTION

Under what circumstances can we make a diagnosis of *Cardiac Infarction*, which in about two-thirds of patients is preceded by a coronary thrombosis?

The diagnosis can usually be suspected on clinical grounds: the persistence of pain, the presence of shock or syncope, the appearance of arrhythmia or heart failure. A fall in blood pressure does not always occur—sometimes there is a transient rise perhaps due to stimulation of medullary vaso-motor centres.

Tachycardia is not invariable—sometimes there is bradycardia due to reflex vagal stimuli or to a degree of heart block. The pain usually makes the patient want to keep still, but I have recently seen two patients who gained some relief by walking about the bedroom.

The electrocardiogram helps in the diagnosis in about 95 per cent of patients in their first attack. Sometimes if a record is taken too soon after the onset, typical changes will not have occurred, but they usually do so within 24 hours. Quite a proportion of infarctions show only on the precordial leads, which may explain why some were missed in the days when only limb leads were taken.

Other aids to the diagnosis are fever which usually occurs within three days, rise of E.S.R. and white cell count, and a rise in the serum glutamic oxalacetic transaminase. This enzyme is present in high concentration in cardiac and skeletal muscle, liver, brain and kidney; death of cells in these organs causes a liberation of enzyme into the blood. The normal level of this transaminase is up to 40 units, and the maximum rise after an infarct occurs between 12 and 48 hours after its onset. The estimation is of considerable value in deciding whether a recent infarction has occurred in a patient who has suffered previous episodes and in whom the E.C.G. is distorted by these or by bundle branch block. It may also help to determine whether an extension of infarction has occurred.

TREATMENT

In discussing the treatment of angina may I remind you that a resident medical officer in Edinburgh, Lauder Brunton, first introduced amyl nitrite to the world in 1867. Eight years later in London, William Murrell (1875) observed the properties of nitroglycerine by using it on himself in out-patients, and he became quite alarmed by its effect!

Treatment of the Attack of Angina

There has been no better trial of drugs for treatment of angina than that of Evans and Hoyle in 1934. They showed without any doubt that glyceryl trinitrate sublingually was the most effective drug for the relief of an attack (86 per cent of patients obtain great relief) and for the prophylaxis of an expected attack (84·5 per cent). No other drug has yet been shown to be more effective. Trinitrin is cheap, (5 shillings per 1000 tablets), reliable, and may be taken as frequently as half-hourly without any complications. It is important to emphasize to our patients that the tablets should be crunched and allowed to dissolve in the mouth. Recently a very stable product has come on to the market so that our supplies are now white rather than chocolate coloured.

Prevention of Angina

Evans and Hoyle showed in their extensive studies that most drugs were ineffective in the prevention of angina pectoris and they pointed the most valuable moral that 40 per cent of patients are improved by a placebo. They tried erythrytol tetranitrate and showed this to be of no value, and I have no reason to differ from their opinion, with regard to the more recent products, Mycardol and Peritrate which are pentaerythrytol tetranitrate. Nor have I found that the use of Praenitrona prevents attacks. There is no evidence that Vitamin E, sex hormones or iodides exert any beneficial effect on the course of the disease. Iproniazid has been found by Towers and Wood (1958) to give relief of pain but has serious toxic effects on the liver and other organs and hence can only be recommended in very severe angina.

In my opinion, the frequency of anginal attacks is best lowered by general measures such as reduction in weight, relief of anxiety where possible (sometimes with the aid of small doses of barbiturates), the avoidance of large meals and exercise after them, resisting the temptation to sweep snow or pull sledges, and a general slowing of the tempo of life, such as dropping a few committees and directorships. Any anaemia should of course be corrected. Trinitrin tablets when sucked before an exercise such as climbing stairs will prevent anginal pain. Nocturnal attacks can sometimes be prevented by patients taking a light supper, sucking Trinitrin when retiring to bed and taking a grain of phenobarbitone, or papaverine. Some advocate depressing the metabolism by anti-thyroid drugs, but the resultant mental and physical slowing may be as unpleasant as the angina.

Treatment of Cardiac Infarction

In treating this condition we are dealing with a patch of dead muscle which may by its presence cause:

(1) an electrically unstable heart leading to ventricular tachycardia or fibrillation which may be fatal,
(2) heart failure,
(3) cardiac aneurysm or rupture.

The aims of treatment therefore are:

(1) healing of the infarct and formation of a firm scar,
(2) the development of collateral blood supply to the surrounding muscle, and possible recanalization of a coronary thrombus,
(3) relief of pain,
(4) correction of hypotension, heart failure and arrhythmias
(5) prevention of thrombo-embolic complications.

Physical and mental rest is essential, and I consider that six weeks in bed, followed by a month's convalescence is advisable with perhaps some remission of sentence for the elderly and second offenders. I think a patient should not be moved in the shocked stage, unless he is in an unsuitable place, such as a train, theatre or the open air, as this may increase the shock and accelerate death.

Usually these people are best nursed in bed, but if they become very breathless, sitting up in a comfortable fireside chair may give most relief. A bedside commode or a sani-chair should be provided and a suitable bed-table to enable the patient to eat, read and write comfortably. A suitcase, hassock or other support for the feet in bed is an aid to comfort and leg movements. An important part of the management is *explaining* the position to the patient so that he is resigned to the period of rest advised and does not "champ against the bit". Provision of adequate interests after the first few days, such as books, radio or a hobby such as sketching or needlework are common sense and need not be glorified by the name "occupational therapy".

Relief of pain is usually effected by morphia, but I would like to commend the use of Pethidine, 150 mgm. and Largactil 50 mgm., certainly in those who vomit after

morphine. Severe pain may last for several days, and these analgesics should not be spared. Thereafter occasional anginal pains may be relieved by Trinitrin. If there is much anxiety, phenobarbitone or amytal may help, and a nightcap of whisky does not go amiss.

Severe hypotension following a cardiac infarct carries a mortality rate of about 80 per cent. Improved prognosis results from the use of pressor agents. The most useful is mephentermine sulphate ("mephine") given intravenously or intramuscularly in doses of 15 to 30 mgms. L-noradrenaline is seldom needed and can only be given in hospital as careful supervision is necessary. But I do not consider the urgent removal of a severely shocked patient in a cold ambulance is beneficial, and wherever possible initial shock should be corrected at home.

Oxygen is widely used for the relief of the cyanosis and shock following an infarction, but there are theoretical objections to its use. In dogs it has been shown that by increasing the difference in oxygen tension between the infarcted and healthy muscle, the heart is made electrically unstable, and the risk of fatal ventricular fibrillation is increased. In consequence, I do not use oxygen unless there is dyspnoea and the patient is obtaining relief from it. One sees only too frequently oxygen being pressed on to a patient with no effect other than to make him struggle.

Digitalis is best avoided in the early days after an infarct unless a fast auricular fibrillation develops with incipient heart failure, when the risks of withholding the drug are greater than the risks of precipitating ventricular tachycardia. If multiple extrasystoles should occur during the course of an infarction, I do not hesitate to use *quinidine* as this may well prevent the development of a fatal ventricular tachycardia or fibrillation.

Should heart failure develop, then we should exhibit diuretics.

Anticoagulants

There is still considerable discussion about the value of these drugs in coronary artery disease. Some still regard them as rat poison, others as the elixir of life. Gilchrist and Tulloch (1956) have shown that the mortality in a large series treated in hospital was halved by the use of anticoagulants. They do not claim that they can prevent heart failure, arrhythmias, or all recurrences. The main benefit is in the prevention of complicating venous thrombosis in the legs which is such a hazard on account of the later risk of pulmonary embolism.

The drawbacks are that:

(1) the drugs need to be started in hospital,
(2) they require frequent laboratory tests for control,
(3) they increase the risk of haemorrhage from silent peptic ulcers, or from the heart causing a haemopericardium.

But there is no doubt in my mind that the benefits of the drugs to a patient in hospital outweigh these disadvantages. All my patients in hospital who have a myocardial infarct receive anticoagulants for the duration of their stay, unless they are very old, or give a history of an active gastric or duodenal ulcer or colitis. The most difficult problem is whether to admit a patient for treatment with "dindevan" or treat him at home. I think the decision can only be made by considering all the factors—age, social condition, mental state, practicability of home nursing, severity of infarct and so on. I do think that patients under the age of 55 should be admitted for anticoagulants. There is increasing evidence that the frequency of recurrence can be reduced by long term anticoagulants. Manchester (1957) treated 204 patients who had suffered infarcts with anticoagulants for from 1 to 10 years and 200 controls with ascorbic acid for the same period. He found the incidence of subsequent infarcts three times greater and the mortality eight times greater in the control group compared with the

treated group. Bleeding complications occurred in only 2·9 per cent. We await with interest the present Medical Research Council trial of this treatment*.

The difficulties of management are great, so I usually compromise and try to keep only those who have suffered more than two infarctions on these drugs indefinitely.

SURGERY OF CORONARY ARTERY DISEASE

In general, a patient with severe coronary artery disease is a bad surgical risk: and major operative procedures are best avoided. Obviously the risk will often have to be taken, for instance when dealing with intestinal or prostatic obstruction.

What I am mainly concerned with is whether surgery has any part to play in the relief of angina. *Thyroidectomy* may occasionally be indicated if a toxic goitre is responsible for cardiac pain, but is not advisable for the relief of angina. *Sympathectomy* of the upper four thoracic ganglia has been practised where intractable pain is a problem. Obviously removal of the warning signal of pain may be dangerous and may tempt the patient to over exert himself but these patients are usually left with a feeling of substernal oppression as warning without frank pain. Benefit from sympathectomy may also come from the blocking of noxious reflexes which result in ventricular fibrillation. Lindgren (1950) gave relief of pain to three-quarters of 105 patients after sympathectomy, but did not claim any prolongation of life thereby.

Another group of operations aims at increasing the amount of blood reaching the heart by means of omental, jejunal, skin or lung grafts or arterialisation of the coronary sinus. O'Shaughnessy (1935) in this country and Beck (1935) in the U.S.A. were pioneers in this field but in general the results were disappointing and the mortality high. Vineberg (1946) in Canada has practised *internal mammary artery implantation* extensively, and in 1955 claimed that half of 30 survivors from the operation were completely or greatly relieved of their symptoms. Others have not so far been able to achieve such good results.

There is no limit to the ingenuity of our surgeons, and recently (1953) Gordon Murray has even attempted excision and grafting of atheromatous sections of the coronary arteries and excision of old infarcts (1947). Another attempted to repair a ruptured interventricular septum. Glover (1957) has practised simple *ligation of the internal mammary arteries* beyond where they give off their pericardial branches with the aim of increasing the blood flow. Although benefit is claimed in 68 per cent, there is considerable doubt of its value apart from it being a powerful mode of suggestion. Mention is made above of Evans and Hoyle's work showing that 40 per cent of patients obtain relief from a placebo.

The most promising field of surgery lies in stimulating the *inter-coronary anastamoses*. As long ago as 1669, a Cornishman, Richard Lower, described these anastomotic vessels. Zoll, Wessler and others in 1951 found these anastomoses in 9 per cent of normal hearts, 63 per cent of hearts with marked coronary narrowing and in 100 per cent where there were old occlusions. Zoll concludes that anoxia is the stimulus for the development of collateral vessels. The post-mortem arteriograms of Fulton (1956) in Edinburgh illustrate how extensive a network of collaterals may be developed in patients with coronary artery disease.

In experimental dogs there is electrical stability when either the heart is uniformly well oxygenated or uniformly cyanosed. But ligation of one coronary artery in a healthy heart or cannulation of one artery with oxygenated blood in a cyanosed heart produced the "current of injury", perhaps more correctly called the "current of oxygen differentials". It is under these circumstances that ventricular fibrillation may arise and the dog or patient "electrocute himself". *Beck's operation* is based on extensive experiments on dogs and aims at the development of sufficient collateral blood supply to prevent these dangerous differentials in oxygen tension. Beck (1935, 1958) has shown

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that most deaths in coronary artery disease are not due to massive infarcts or heart failure, but are from serious disturbances of rhythm, particularly ventricular fibrillation. This is supported by coroners' pathologists who frequently find in cases of sudden death that there is only early coronary artery disease and no obvious infarction. Dr. N. J. Brown tells me that in 100 consecutive post mortems for sudden deaths which were attributable to coronary artery disease, large infarcts were found in only 55, and recent thrombosis in only 58. Beck's operation consists of partial ligation of the coronary sinus, abrasion of the pericardium and insertion of asbestos powder. It should be emphasized that it has no effect on the underlying atheroma. In the last 347 cases operated on by Beck, there was a 6 per cent operative mortality, and of the survivors 32 per cent had great relief and 62 per cent moderate relief of cardiac pain. This 94 per cent were able to resume work. Mr. Michael Wilson who was trained by Beck, has done a few of these operations in Bristol. Obviously at first we have only offered the operation to those most seriously afflicted, and hence with the worst prognosis, but there have been several who have derived great benefit. One of these was a 61-year-old housewife who had such severe angina that she was confined to her room. A Beck operation was performed two years ago at Southmead Hospital and she is now able to enjoy a normal social life, going for walks of up to a mile.

It is my opinion that a patient should be considered for surgical treatment if he has incapacitating angina, providing he has no cardiac enlargement, hypertension, heart failure or evidence of recent infarction.

PROPHYLAXIS

As individual doctors, and indeed potential patients ourselves what should we advise?

(1) Take regular physical exercise, but resist the temptation to do the work of a bulldozer after months of hibernation.

(2) Watch your vital statistics—don't dig your grave with your teeth.

(3) Don't give the Chancellor of the Exchequer a surplus in excise tax by your consumption of tobacco.

(4) What may be the most important factor—choose your parents carefully!

SELECTED REFERENCES

Barritt, D. W. (1956). *Brit. Med. J.*, **2**, 640.

Beck, C. S., Leighninger D. S., Brofman, B. L., and Bond, J. F. (1958). *J. Amer. Med. Ass.*, **168**, 2110.

Beck, C. S., Tichy, V. L., and Moritz, A. R. (1935). *Proc. Soc. Exper. Biol. & Med.*, **32**, 759.

Bronte Stewart, B., Keys, A., and Brock, J. F. (1955). *Lancet*, **2**, 1103.

Brown R. G., Davidson, L. A. G., McKeown, T., and Whitfield, A. G. W. (1957). *Lancet*, **2**, 1073.

Brunton, T. L. (1867). *Lancet*, **2**, 97.

Duguid, J. B. (1946). *J. Path. Bact.*, **58**, 207.

Eindhoven, W. (1903). *Pflugers' Arch. F.d. Physiol.*, **99**, 472.

Evans, W. and Hoyle, C. (1934). *Quart. J. Med.*, **27**, 105.

Fullerton, H. W., Davie, W. J. A., Anastasopoulos, G. (1953). *Brit. Med. J.*, **2**, 250.

Fulton, W. F. M. (1956). *Brit. Heart J.*, **18**, 341.

Gilchrist, A. R. and Tulloch, J. A. (1956). *Scot. Med. J.*, **1**, 1.

Glover, R. P. (1957). *J. Arkansas Med. Soc.*, **54**, 223.

Greig, H. B. W. (1956). *Lancet*, **2**, 16.

Hammond, E. C. and Horn, D. (1954). *J. Amer. Med. Ass.*, **115**, 1327.

Harvey, W. (1649). *Exercitatio Altera.* Frankfurt.

Heberden, W. (1768). Lecture at R.C.P., London, 21st July.

Jenner, E. (1827). *Life of, J. Baron*, **1**, 39.

Keys, A. (1953). *J. Mt. Sinai Hosp.*, **20**, 118.

Kinsell, L. W., Partridge, J. W., Boling, L. A., Balch, H. E., and Cochrane, G. C. (1952). *J. Clin. Endocrin. & Metab.*, **12**, 909.

Lindgren, I. (1950). *Acta Med. Scand.*, **138**, (suppl. 243), 1.
Lower, R. (1669). *Tractatus de Corde*, London.
Malhotra, R. P. and Pathania, N. S. (1958). *Brit. Med. J.*, **2**, 528.
Manchester, B. (1957). *Ann. Intern. Med.*, **47**, 1202.
Master, A. M., Dark, S., and Jaffe, H. L. (1939). *Amer. Heart. J.*, **18**, 434.
McDonald, L. and Edgill, M. (1957). *Lancet*, **2**, 457.
McDonald, G. A. and Fullerton, H. W. (1958). *Lancet*, **2**, 600.
Medical Research Council (1959). *Brit. Med. J.*, **1**, 803.
Merskey, C. and Nossel, H. L. (1957). *Lancet*, **1**, 806.
Morris, J. N. and Crawford, M. D. (1958). *Brit. Med. J.*, **2**, 1485.
Murrell, W. (1875). *Lancet*, **1**, 80, 113, 151, 225.
Murray, G. (1953), (1947). *Ann. Surg.*, **126**, 523.
O'Brien, J. R. (1957). *Lancet*, **1**, 1213.
Oliver, M. F. and Boyd, G. S. (1956). *Lancet*, **2**, 1273.
O'Shaughnessy, L. J. (1935). *J. Thorac. Surg.*, **5**, 386.
Pardee, H. F. B. (1920). *Arch. int. Med.*, **26**, 244.
Parkinson, J. and Bedford, D. E. (1927), *Heart*, **14**, 195.
Parry, C. H. (1799), Sycope Anginosa, Bath.
Robertson, W. B. (1959). *Lancet*, **1**, 444.
Towers, M. K. and Wood, P. (1958). *Brit. Med. J.*, **2**, 1067.
Vineberg, A. (1946), (1954). *J. Int. Coll. Surg.*, **22**, 503.
Yudkin, J. (1957). *Lancet*, **2**, 155.
Zoll, P. M., Wessler, S., and Blumgart, H. L. (1951). *Amer. J. Med.*, **11**, 331.

A PATHOLOGIST'S SURVEY OF SUPERFICIAL TUMORS REMOVED IN A CASUALTY DEPARTMENT*

T. F. HEWER

Professor of Pathology, University of Bristol.

The Casualty Department of a large hospital provides a fascinating collection of clinical material, ranging as it does from street accidents and sudden severe medical or surgical illness to the patient who wishes to have a minor cutaneous blemish removed for cosmetic reasons. It is especially the people in the last category and those with less trivial but apparently minor superficial lesions who provide a wealth of varied problems for the diagnostic histology department. Fortunately it is the custom to send all such tissue for examination.

From the pathologist's point of view these superficial lesions provide a most interesting diagnostic exercise. Some idea of the variety can be obtained by scrutiny of the list (Table 1) which represents the specimens received in twelve months. They are listed not in order of frequency but in groups of more or less related conditions; the number of examples of each is indicated alongside.

TABLE I

Diagnosis	No. of Specimens
Inflammatory	23
Epithelial hyperplasia, not primarily inflammatory	5
Epidermal cyst	23
Keratosis senilis	2
Squamous papilloma	38
Cornu cutaneum (sebaceous wart)	2
Squamous carcinoma	14
Basal cell carcinoma	22
Verruca vulgaris	8
Verruca plantaris	2
Molluscum sebaceum (= pseudocarcinomatosum)	4
Benign calcified "epithelioma"	4
Molluscum contagiosum	1
Fibro-epithelial polyp	9
Benign sweat gland tumour	1
Malignant sweat gland tumour	1
Secondary carcinoma	5
Benign melanoma	24
Malignant melanoma	6
Blue naevus	1
Benign juvenile melanoma	1
Histiocytoma (sclerosing angioma)	4
Haemangioma	18
Lymphangioma	1
Lipoma	22
Neurofibroma	15
Sarcoma (five being neurofibrosarcoma)	6
Leiomyoma	2
Keloid	5
Foreign body granuloma	2
Other Lesions	11
Total	282

* Originally written for the Report of the South Western Regional Cancer Records Bureau and reproduced with permission of the Director.

This material came from the Casualty Department of the Bristol Royal Infirmary.

The epidermal cysts included eight sebaceous cysts but the remainder were a very mixed bag; there were a few implantation dermoids but several were simple cysts with no sebaceous glands alongside, lined by degenerate squamous epithelium and containing desquamated keratin and amorphous debris which did not appear sebaceous in the gross. Some of these were doubtless due to obstruction of sweat glands, irregular hair follicles and other disorders of epithelial adnexa and all were unmistakably benign.

An observation often made in the laboratory is that a large number of excised cutaneous lesions are described on the report form as sebaceous cysts. They are generally sent unopened—and we prefer to receive them like that—and in consequence it is not easy to determine at the time of excision whether they are cystic or solid. This point is worth mentioning because there must be occasions in practice where a rounded subcutaneous tumour which appears cystic may in fact be a carcinoma metastasis or one of the many forms of sub-epidermal basal cell carcinoma.

The squamous papillomata seldom gave much difficulty in diagnosis and the same was true of the benign calcified "epitheliomata" although the latter condition is notoriously apt to be misleading and trap the unwary into making a false diagnosis of malignancy.

Molluscum sebaceum or, as it is often called, kerato-acanthoma or—another synonym—molluscum pseudocarcinomatosum is a condition that always causes the histologist anxiety. It grows rapidly, in a few weeks, and forms a rounded projecting epithelial tumour with central keratinization. Quite miraculously it regresses in a few more weeks and leaves a scar. Histologically it is often impossible to be certain that it is not a true squamous carcinoma and consultation with the clinician is essential for an accurate diagnosis.

The melanomata are an important and interesting group. Some of the benign ones were removed for cosmetic reasons but most on suspicion of malignancy. The benign juvenile melanoma, of which only one example appeared in the year under review, is sometimes mistakenly reported as malignant on account of its quite alarming histological appearance.

Among the more difficult specimens for diagnosis were the small lesions removed from eyelids. The ophthalmic surgeon is faced with peculiar difficulty in removing the whole of a lesion on the lid margin and when the excision is for a diagnostic biopsy the tendency is, very properly, to be conservative. Not infrequently the specimen in such cases consists of a slice of keratinizing epidermis with no indication of the junction with the dermis.

Routine histological examination of every piece of tissue removed in Casualty, in Out-Patients or in the general practitioner's surgery is a most necessary precaution. One hopes that the Regional Cancer Records Bureau will always be informed when one of these lesions proves to be malignant or equivocal because a follow-up in such cases is of the highest importance. This is perhaps particularly true in the case of the basal cell carcinomata, since they may not have been completely removed, and the malignant melanomata because these latter are not necessarily as malignant as their reputation suggests and careful observation with prompt dissection of lymph nodes at the first appearance of a recurrence may well be a life-saving measure.

I think the most important point arising from a survey of material such as this is that there are numerous conditions on the borderline of malignancy: many of them are reported as benign and even when uncertainty is expressed by the pathologist I fear that the case is not reported to the Cancer Bureau. I am sure a lot of patients are thus lost sight of and I suggest that an improvement in the procedure of follow-up is overdue.

POST-PARTUM NECROSIS OF THE PITUITARY

A Clinical Pathological Conference of the University of Bristol Medical School on 5th May, 1959, P.M. 6038

CHAIRMAN: PROFESSOR T. F. HEWER

Dr. J. E. Cates: In 1954, at the age of 58, this woman was admitted into the United Bristol Hospital under the care of Mr. Pocock as an emergency. She came in with bellyache, and her doctor said in a letter that he thought she might have acute intestinal obstruction. For the last few months she had been short of breath on exertion and had been tired and the house surgeon noted that there were some physical signs in the chest, including decreased movement on one side, and there was difference in breath sounds. A chest X-ray showed that the patient had a very large cavity which is considered to be consistent with chronic pulmonary tuberculosis. (See Plate I.)

When I saw her, she presented an astonishing picture: a pale wizened apathetic woman looking a lot older than her years, with no hair in her axillae and virtually none on her pubis; the photograph (Plate II) was taken a little later on, when she was feeling better. She had married when 31 and at the age of 37 she had her first and only baby, a boy. She had a very difficult time with severe haemorrhage afterwards and shortly after that she alleged (wrongly) that there had been so much trouble that her uterus was removed. In fact she did have a uterus, as you will see from the post-mortem notes, but she did not have any more children or periods. She hated the cold and was apathetic and miserable and did not take much interest in what was going on about her. These facts all pointed to her having what we call Sheehan's syndrome (or post-partum pituitary necrosis). She had however escaped three fates which may befall people with anterior pituitary necrosis. She had not been submitted to anaesthetic and been killed, her condition had not been mistaken for pernicious anaemia and treated, nor had it been diagnosed as myxoedema and treated with thyroid.

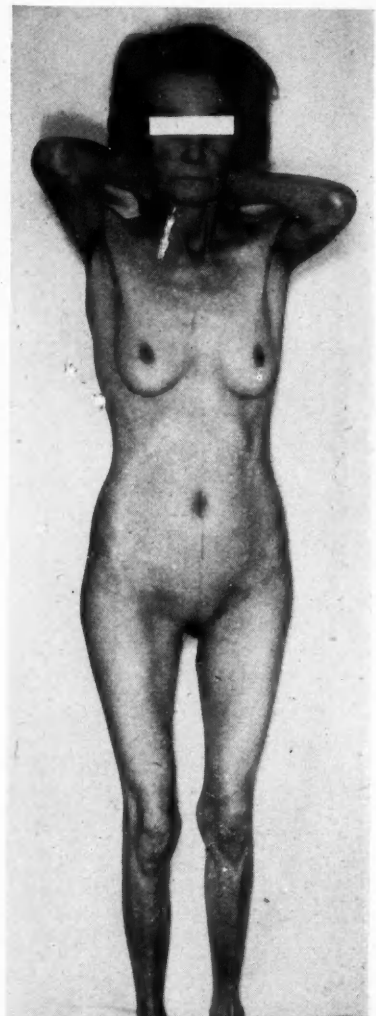
In spite of her feeble state she did not seem to have *active* tuberculosis, she had no cough, no sputum, she was not coughing up blood and there was no history to suggest active tuberculosis in the past. There was no history of contact. On clinical examination she was not running a fever. Although scraggy, she had not lost weight; she had not been sweating. There was no clubbing and I could not get any sputum out of her at the bedside. The physical signs were in keeping with the X-ray; the movement was down on this side; the trachea was pulled over. Her vocal fremitus was increased and percussion note is noted to have been decreased. There was bronchial breathing over the area corresponding to the cavity shown on the X-ray; there was no post-tussic suction. B.P. was 150/80. All the sputum was negative for tubercle bacilli, and six stomach washings were likewise negative, so I asked Dr. Pearson to see the patient and he thought "she has a very chronic fibroid disease of the upper zone, definitely tubercle—quite likely burnt out. She also had scanty rales at the left base where X-ray also shows some fibrosis". He suggested tomography for further views of the cavity. The tuberculosis therefore did not seem to be active and certainly not infectious so we turned our attention to the endocrine disturbances. Incidentally during the remaining four-and-a-half years of her life her chest was X-rayed every six months and the appearances remained unchanged.

So to return to the picture of panhypopituitarism: we found that she had gross disturbance of electrolytes which is unusual in a pituitary disorder of this nature. Her serum sodium was 113 Meq./L, a very low figure, and her urine sodium was high, 118 at Meq./L, which findings together are very good evidence of suprarenal deficiency. There are many causes of a low sodium but if you find that the kidney is squandering

PLATE I

X-Ray of chest showing cavitation and fibrosis at the right apex.

PLATE II



Showing absence of axillary and pubic hair.

sodium when the body is short of it you suspect that there is poor function of the suprarenal cortex. The urinary cortico-steroid output was estimated four times and was under 1 mg. for 24 hours. Her thyroid function was decreased; her B.M.R. was 33 per cent. Her E.C.G. was abnormal with *T* waves flat in leads 2 and 3, and low voltages, both of these suggesting that she was hypothyroid.

Another possibility was that if she had tubercle she could have Addison's disease; but X-ray showed no calcification in her suprarenals and the ACTH test for eosinophils, for what it is worth, showed a profound drop. At that time we were not relying on the effect of ACTH on the steroids in urine (we were still studying our methods); I would do this steroid test nowadays for it is the best way to determine whether the suprarenal failure is primary or secondary.

There was also a possibility that she migh have a tumour in her pituitary fossa but X-ray showed no evidence of this, neither was there any "neighbourhood" sign or symptom—she had no alteration of her visual fields and no symptoms of headache and so on. So we concluded that after her large post-partum haemorrhage she suffered necrosis of most of her anterior pituitary gland.

As her serum sodium was low she was given 1 g. of sodium chloride t.d.s., together with cortisone acetate with a modest dose of 25 mgm twice daily; she did not respond appreciably so the dose was increased to 25 mgm. three times a day and then suddenly the picture changed completely: from being apathetic and docile, dull, pale, she became maniacal. She picked up jugs from which she was fed by nurses and smashed them against the wall, and really alarmed everybody; she also became persecuted—a dramatic change with just a few grammes of cortisone. So Dr. Barbour was called in; he was most interested. Cortisone was stopped and she was sent out on extra salt by mouth only, and we watched her in out-patients' department. It was soon quite clear, however, that she needed steroid treatment because within a few weeks she became even more depressed and apathetic again and developed for the first time what is a really dangerous complication with hypopituitarism, namely diarrhoea. The danger is that diarrhoea is a drain on the salt and water reserves of the body and imposes a strain on the ineffectual suprarenals. When other patients with panhypopituitarism have gone into a coma there has often been preceding diarrhoea. She was re-admitted and started on 6·25 mg. of cortisone b.d., and because she was post menopausal and skinny we gave her melthyl testosterone, 10 mgm. a day, and thirdly, because she was still squandering her salt I gave her a D.O.C.A. implantation. To cut a long story short, each time she was seen in the endocrine clinic after that she was remarkably well, cheerful, active and physically very much better. Her electrolytes were almost satisfactory, and apart from an episode in which she was discovered to have broken ten ribs, presumably from cough fractures, in 1956, her course was eneventful until just before she died. On the day of her death, doctor rang and said "Mrs. L. with panhypopituitarism has got a chest infection and is very poorly, will you admit her?" I said "send her in an ambulance". She was sent straight in, but she died in the corridor between the surgical and medical blocks as she was being admitted.

All patients with suprarenal deficiency from any cause are taught that they need a much larger dose of cortisone during a severe infection. This lady seems to have died within a few hours of becoming ill.

Professor Hewer: Has anyone any questions for Dr. Cates at this stage?

Question: Was she treated with thyroid extract and what is your view of this treatment?

Dr. Cates: No. She did not need it clinically.

Question: Did you put her on streptomycin?

Dr. Cates: No. There was no evidence that she had active tubercle.

Question: Is cortisone therapy likely to re-activate the tubercle?

Dr. Cates: If you give cortisone in what is dramatically called "poisonous doses" to suppress say, rheumatoid arthritis, patients are more likely to develop infection, but where you are just replacing their day to day needs, then they are in no more danger of this than we are.

Dr. Allwood: What was her E.S.R.?

Dr. Cates: In 1954 she had a Hb of 70 per cent; E.S.R. 38.

Question: Is there any advantage in giving A.C.T.H. to this patient.

Dr. Cates: No. A.C.T.H. is a protein and proteins stimulate the production of antibodies so A.C.T.H. may lose its effect and moreover, prolonged A.C.T.H. treatment is more expensive. Lastly if you give replacement treatment it is not an injection and patients prefer it.

Question: Was not her blood pressure unexpectedly high throughout her first hospital admission?

Dr. Cates: Yes, but it went up very much higher when she was treated; it went up to 220/100 when she was "normal" later on.

Question: Did she then have hypertension?

Dr. Cates: I think she was a hypertensive woman. Her B.P. fell to 150/80 when she was ill.

Dr. Betteridge: We heard what her general appearance was like before she commenced treatment. As a result of treatment she did have some quite reasonable amount of pubic hair; she had some axillary hair, her eyebrows were quite complete and the hair of her head was not at all sparse. However, she was very thin. She was 5 ft. tall but she weighed just 5 stones, which is well below her expected weight. Another point of interest was that the pigmented areas, which are normally said to be de-pigmented in cases of panhypopituitarism, were in fact now normally pigmented.

The pituitary gland was small with obvious loss of anterior lobe substance. The posterior lobe appeared normal. Microscopically there was only a small fraction of functioning anterior lobe present, lying just in front of the pars intermedia. There were no acidophils present and few basophils, many of which were hyaline. Chromophobe cells were present and appeared normal.

The adrenal glands were small, as might be expected, their total weight being 4·5 g., compared with an expected weight of over 7 g. On section the cortex was seen to be reduced to between 0·4 and 0·8 mm. in thickness and contained a moderate amount of lipid. Microscopically there was thickening of the capsule with some fibrosis in the zona glomerulosa, which alone of the zones of the cortex could be recognized with any certainty since there was general disorganization of the cortex. In some areas the zona glomerulosa could be recognized adjacent to the medulla which was itself normal.

The thyroid gland weighed only 7 g., just about a quarter of the normal expected weight, and was flattened and fibrous in appearance. Microscopically there was a considerable diffuse fibrosis present without round cell infiltration. The acini were lined by flattened cuboidal epithelium and contained colloid.

The heart weighed only 180 g. and was reduced in size but otherwise was externally normal. There was very little atheroma present in the main vessels and the aorta itself was surprisingly elastic. Microscopically the heart muscle fibres were small and contained lipochrome pigment and a little fat.

The liver was greatly reduced in size, weighing only 695 g. The cells appeared reduced in size microscopically.

The kidneys (weight 105 and 100 g.) were normal with no evidence of arteriosclerosis. The uterus was present and atrophic, as were the ovaries.

The other main findings of interest in this case were in the lungs. The left pleural cavity was obliterated by hard fibrous adhesions in its upper part; in the lower part there were recent soft fibrinous adhesions with loculi of clear serous fluid. The upper

lobe of the left lung showed marked old apical fibrosis, and the so-called "sugar icing" appearance of thickened hyaline visceral pleura extending into the interlobular fissure. The lower lobe showed scattered areas of old fibrosis and recent bronchopneumonia. The right pleural cavity was obliterated by firm adhesions. The right lung showed a similar thickening of the visceral pleura of the upper lobe which was itself entirely replaced by old thick-walled cavities which contained thick creamy flocculent material. Two of the cavities were shown to communicate with bronchi which showed a moderate degree of bronchiectasis. The little lung tissue present was fibrous. The middle lobe showed a confluent pneumonia and the lower lobe had areas of old fibrosis and recent bronchopneumonia similar to that seen in the left lower lobe. The microscopical appearances of the old lesions and the cavities were of non-specific fibrosis. There was no unequivocal evidence of tuberculosis. No tubercle bacilli were present. Culture of the lungs revealed a good growth of pneumococci.

In short, this was a woman who survived post-partum necrosis of the anterior lobe of her pituitary to show the features of panhypopituitarism with secondary deficiency of other endocrine glands. It is interesting to note the absence of cardiac hypertrophy and renal lesions in the presence of a sustained hypertension. Her chronic chest condition had all the feature of a tuberculous process which had "burnt out", and she died finally of an overwhelming pneumococcal bronchopneumonia.

Professor Hewer: Dr. Cates, what is your interpretation of the blood pressure reading. I believe the highest diastolic blood pressure recorded was 105, would you be inclined to call this hypertension with a systolic pressure of 180 at one time?

Dr. Cates: It was above that figure. I would agree with you that she had hypertension. Some of the other patients with pituitary failure on replacement therapy had had high blood pressure. It may be that we have not yet struck the right balance of hormone replacement.

Professor Hewer: I would like to follow up that question by asking whether cortisone was responsible for what rise there was.

Dr. Cates: It may well be so. She was a small woman and was otherwise sensitive to normal therapeutic doses.

Her fractured ribs are interesting. Dr. Betteridge did not mention that; but in pituitary necrosis the lack of androgens from the suprarenals and oestrogens from the ovaries in a woman can lead to decalcification, for that reason we gave her small doses of testosterone. Dr. Betteridge, can you tell us whether the bone has been examined?

Dr. Betteridge: Yes, sections of a vertebra and of the ribs show definite evidence of osteoporosis.

Professor Hewer: It is a pretty classic example, is it not, of pituitary necrosis, following post-partum haemorrhage and the panhypopituitarism which follows.

Dr. Cates: Yes. Presumably with just enough anterior pituitary gland remaining, 10 per cent or so, to keep her alive, just enough to prevent complete failure of her suprarenals and thyroid. If the pituitary is completely destroyed patients do not live long.

News from Societies

WEST OF ENGLAND CHILD HEALTH GROUP

Secretary: Dr. A. L. Smallwood, Department of Public Health, Tower Hill, Bristol 2

10th Dec., at 8.30 p.m.: M. B. Lennard, Esq., M.V., CH.B., **"Family Practitioner Problems and Domiciliary Care".**

7th Jan., at 5.30 p.m.: Mrs. J. Madders, **"The Application of Physiotherapy in Special Needs".** In the Small Physics Lecture Theatre at the Royal Fort.

18th Feb., at 5.30 p.m.: H. C. Trowell, Esq., O.B.E., M.D., F.R.C.P., **"Paediatrics in the Tropics".**

10th Mar., at 8.30 p.m.: Miss Suzanne K. R. Clarke, M.D., **"Delinquency among Orphan Viruses".**

7th May, Visit to the Cotswold School, Ashton Keynes, nr. Swindon: C. A. Joyce, Esq., M.B.E., M.A., Headmaster.

Meetings are held in the Department of Child Health Lecture Theatre at the Children's Hospital, unless otherwise stated.

B.M.A. (Barnstaple Division)

Secretary: Dr. S. G. Brook, Eddleston, Park Lane, Barnstaple

Dec. (date to be arranged): **Clinical Meeting** at the North Devon Infirmary in conjunction with the South-Western Branch.

20th Jan., at 8.30 p.m.: Professor C. Bruce Perry, M.D., F.R.C.P., **"Iatrogenic Disease, or the Hazards of Modern Therapy".** At the North Devon Infirmary.

PLYMOUTH MEDICAL SOCIETY

Secretaries: Dr. Hugh Jolly, Yennadon House, Yelverton, and Dr. Bernard Peck, 5 Lockington Ave., Hartley, Plymouth

11th Dec., at 8.30 p.m.: **Clinical Evening** at the Royal Naval Hospital.

15th Jan., at 8.30 p.m.: Robert V. Cooke, Esq., CH.M., F.R.C.S., **"Bees in My Bonnet",** at Freedom Fields.

5th Feb., at 8.30 p.m.: **Clinical Evening** at Freedom Fields.

19th Feb., at 8.30 p.m.: **"Medicine and the Law".** Joint discussion meeting with the Incorporated Law Society of Plymouth. At Freedom Fields.

4th Mar., at 8.30 p.m.: P. D. Trevor-Roper, Esq., M.A., F.R.C.S., **"The Influence of Eye Disease on the Artists".** At Freedom Fields.

13th April, at 2.30 p.m.: Visit to Plymouth City Water Works.

9th May, at 8.30 p.m.: **Annual General Meeting** at Greenbank.

Notes and News

Professor R. Milnes Walker has been appointed a member of the Medical Research Council.

Dr. Percy Stocks has been awarded the Bisset Hawkins medal of the Royal College of Physicians.

Dr. Kenneth Bergin has been elected master of the Guild of Air Pilots and Air Navigators for 1959–60.

Obituary: Dr. J. E. Lucas.

Appointments

UNITED BRISTOL HOSPITALS

May–November 1959

Name	*Appointment*	*Formerly*
LYON, D. G., PH.D., L.D.S., F.D.S.R.C.S.	Hon. Consultant Dental Surgeon (during tenure of post of Lecturer in Dental Surgery in the University of Bristol).	Senior Registrar status.
STEPHENSON, J. C., B.D.S., F.D.S.R.C.S., D.ORTH.	Senior Registrar in Orthodontics.	Senior Registrar, Eastman Dental Hospital.
SOLOMONS, D., M.B., B.CH., F.R.C.S.(EDIN.).	Registrar in Surgery.	Registrar, St. Catherine's Hospital, Birkenhead.
BHOWES, J. B., M.B., B.S.	Registrar in Anaesthetics.	S.H.O. in Anaesthetics, U.B.H.
WILKINS, J. L., M.B., B.S., D.C.H.	Registrar in Paediatrics.	Registrar in Paediatrics, South Devon and East Cornwall, H.M.C.
FRASER, I. D., M.B., CH.B.	Registrar in Pathology.	Resident Clinical Pathologist, B.R.I.
WILLS, M. R., M.B., CH.B.	Registrar in Pahtology.	Junior Clinical Pathologist, B.R.I.

Dr. G. W. Burton, Lecturer in Anaesthetics in the University of Bristol, has been accorded the honorary status of Senior Registrar with the United Bristol Hospitals during the tenure of his University appointment.

Dr. K. R. Gough, Research Fellow in Medicine to the University of Bristol, has been accorded the honorary status of Registrar with the United Bristol Hospitals during the tenure of his University appointment.

SOUTH WESTERN REGIONAL HOSPITAL BOARD

August–November, 1959

Name	*Appointment*	*Formerly*
	BRISTOL	
MISHRA, N., M.M.F. (CALCUTTA), D.T.M. & H. (ENG.).	Registrar in Diseases of the Chest, Bristol Chest Clinic/Ham Green.	J.H.M.O., Ham Green Hospital, Bristol.
APSIMON, H. T., M.B., CH.B. (BRISTOL), D.OBS.R.C.O.G.	Medical Registrar, Frenchay Hospital.	S.R.M.O., Frenchay Hospital.
	BATH	
CANNICOTT, S. M., M.A., M.B., B.CHIR.(CANTAB.) D.P.M. (CONJOINT)	Assistant Psychiatrist, Mendip Hospital, Wells.	Senior Registrar, Holloway Sanatorium.
NEATBY, G. M., M.A., M.R.C.S., L.R.C.P., D.O.M.S.	Ophthalmologist, Bath Clinical Area.	Clinical Assistant in Ophthalmology, Bath Eye Infirmary.
O'FLYNN, B.P., M.B., CH.B., B.A.O. (N.U.I.).	Registrar in Pathology to the Bath Group of Hospitals.	Registrar in Pathology, Bath Group of Hospitals.

SOUTH SOMERSET

Name	*Appointment*	*Formerly*
AKEHURST, A. C., M.B., B.S.(LOND.),F.R.C.S. (ENG.).	Consultant General Surgeon, South Somerset Clinical Area.	Senior Surgical Registrar, B.R.I.

NORTH GLOUCESTERSHIRE

HART, R. J., M.A., M.B.B.S. (LOND.), F.R.C.S. (ENG.).	Consultant Orthopaedic Surgeon North Gloucestershire Clinical Area.	Senior Registrar, Royal National Orthopaedic Hospl.
LLOYD, T. W., D.M., B.CH.(OXFORD), M.R.C.P. (LOND.).	Consultant Physician Geriatrician, North Gloucestershire Clinical Area.	Physician Superintendent, St. Wulstan's Hospital.
WALKER, D. L., M.D.(LOND.). D.P.M.	Consultant Psychiatrist Medical Superintendent, Horton Road and Coney Hill Group of Hospitals.	Assistant Psychiatrist, (S.H.M.O.) Netherne Hospital, Coulsdon, Surrey.
BLATCHLEY, W. M.B.B.S.(LOND.)	Clinial Assistant to the Rheumatism Clinic in Gloucester. (Reappointed.)	

DEVON AND CORNWALL

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DOMESTIC HAZARDS WITH NEUROLOGICAL SIGNIFICANCE

BY

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It is not the purpose of this paper to discuss what Dr. Boucher of the Ministry of Health has emphasized—the frequency of accidents in the home from slippery floors, hot water burns or electric fires, but to consider the more unusual domestic hazards which arise in the house or garden, with an emphasis on the neurological effects they produce. Most families have drugs of some kind in the house, which may be considered non-toxic, such as iron. It is well known that iron tablets have killed some children, for the child can mistake the pretty coloured tablet for a sweet and take an overdose of iron. It is the less obvious hazards I wish to deal with here.

Metallic Poisonings

In this modern age, in which new chemical compounds are frequently introduced, particularly for food preservation and cleansing, it is always possible that some new compound may be introduced which has considerable toxicity, either immediately or from its cumulative effect. About three years ago in France, a compound, to be taken orally containing organic tin, was passed as safe for the treatment of boils. It was only after nearly a hundred people had died from its effects that it was realized that the material was highly toxic, and compensation claims are still being settled. If a compound can be put on the market so easily in France, it must be realized that a similar predicament might arise in this country, before the toxic effect of a substance is realized. It took us well over a generation to associate Pink Disease in children with mercury present in teething powders. It is now generally accepted that this mercury compound was responsible for the polyneuritis and rash in this disease of children. These are but two examples of how chemical compounds, apparently innoxious, can be accepted. Heavy metals have always produced poisoning and usually give symptoms which are neurological. Organic mercury has been used as dressing for seeds and Hunter and Russell[1] described cases of poisoning from this substance which produced a specific damage to the cerebellum and the occipital lobes, producing an occipital lobe blindness.

Mercury has produced poisoning in police detectives who used mercury as finger print powder, and also in meter readers who handle the mercury in the course of their work. Symptoms produced in these cases are different from those of organic mercury as they were mainly depression, anxiety and the classical tremor. Many of them were thought to be psychological cases before it was realized that they contracted their trouble as a result of handling mercury.

Lead as a cause of domestic poisoning has been known for a long time. It is not always realized that lead can still produce poisoning n this modern age, producing a variety of symptoms such as encephalopathy with fits, coma and mental derangement, wrist drop, jaundice and colic. One of the earliest descriptions of lead poisoning was that of Sir George Baker[2] in 1767. He showed that lead poisoning was produced, in Devonshire, by the storing of cider in lead containers, and he also indicated that in Worcestershire, where wood casks were used, no poisoning occurred. Having attacked a local interest he was denounced from the pulpit for interfering with the cider industry. It is perhaps poetic justice that two years ago a case of severe lead poisoning

was admitted from Devonshire to the neurosurgical unit at Frenchay. This was a woman whose symptoms were originally thought to be due to an intracerebral tumour and who had actually had a decompression for her cerebral symptoms two and a half years before. She was again admitted with signs of very high intracranial pressure, fits, mental disorder and jaundice. Mild punctate basophilia in her blood give a clue to the diagnosis and treatment with di-sodium versenate, a new chelating agent, produced a dramatic recovery of symptoms and within eight days her papilloedema had disappeared, her mentality became normal and she returned home perfectly well. After communicating with the local medical officer of health at Torrington, it was discovered that this patient lived on a farm in which pipes from a well were all lined with lead, and as the water was acid, the patient had continuously absorbed the lead for the past twelve years. Her husband and daughter were also found to have a high lead content in their blood, although they had so far suffered no ill effects. The whole water supply was altered, the lead piping being replaced by plastic pipes, at considerable cost to the local authority. The patient has remained perfectly well since this date, but it is of course possible that her daughter and husband may at a later date show symptoms when their bones decalcify. This shows that even in this country the water supply may still be contaminated with lead. Other sources of lead poisoning which have recently been described: cases of lead poisoning, a few of them fatal, occurred in the North of England when lead batteries were burned as a source of fuel in stoves for heating purposes. Lead fumes were produced and several children died. Children also get lead poisoning from licking lead paint on toys and there was a severe outbreak of lead poisoning in Queensland owing to dust from lead painted railings flaking off in a hot summer. In at least one case lead poisoning has been produced by lead paint used by actresses; poisoning from lead nipple shields and lead containers for iced lollies has been described. The lead poisoning produced by tetra-ethyl petrol produces a neurological picture but is hardly a domestic hazard.

McAlpine[3] has recently suggested that metallic poisoning may be produced indirectly by eating fish or animals that have themselves consumed a noxious compound. The discharge of factory effluents has been suggested as the cause of an obscure outbreak of poisoning in Japan, where a considerable number of fishermen and people living in the vicinity of a coastal town in Japan were affected with ataxia, blindness and motor weakness. The source of the poisoning was traced to the fish that these people ate. Crows and domestic animals also died. The first possibiity is that the effluents from a local chemical factory was discharged in a different place nearer the coast or secondly that it was due to a large amount of ammunition that had been dumped into the sea after the war, in this area, which contained a high metal content. The metals suspected originally were beryllium and selenium, neither of which has been known to produce much toxic effect on the nervous system. A recent communication from Japan appears to incriminate mercury as being the likely cause of the poisoning. The clinical signs of these cases would fit organic mercury poisoning much more easily than any of the other metals suggested.

Thallium is also a nerve poison, producing peripheral neuritis and optic atrophy, but it is not a metal which people use much and it is only used medicinally in the treatment of ringworm.

Insecticides

Since the recent war there has been a larger and larger use of insecticides, both domestically and in agriculture. The commonest insecticide used is of course, D.D.T. It is not regarded as being acutely toxic and very few cases of definite poisoning in man have occurred, except by suicidal intent. It is, however, a nerve poison and acts on the insect by paralyzing the nervous system. In certain cases of poisoning in man it has produced a polyneuritis, and liver and kidney damage. It is a cumulative drug and is

stored in fat. In a recent analysis of 50 women in America, taken at random, 35 were found to contain considerable quantities of D.D.T in their fat, which had accumulated merely as a result of domestic exposure to D.D.T., by using fly sprays and other compounds. We cannot tell whether this drug will have cumulative effects over a long period. It has been shown that young animals are much more susceptible to its toxic effects than adults, and after spraying pastures calves were found to be prone to epileptic fits. It is more dangerous in an oily solution used as woodworm killers because it is rapidly absorbed through the skin. These oily preparations have been known to produce polyneuritis when the person concerned has used them without due care, and absorption has taken place through the unprotected skin. Polyneuritis has resulted and this may be due either to D.D.T. or to pentachlorophenol which also has been found to produce polyneuritis in workers who make the compounds[4].

More toxic insecticides are used in agriculture. Organic mercurial derivatives have already been mentioned; the dinitro-orthocresol derivatives are highly toxic, usually producing poisoning in people who use the sprays without due precaution, producing rapid increase in basal metabolic rate, rapid pulse rate, sweating and collapse.

The organic phosphorous compounds are also highly poisonous producing paralysis at the neuromuscular junction. Luckily, however, atropine is an effective antidote. If the crops are gathered too soon after spraying, say anything less than three weeks after exposure, particularly in a dry summer, there is a risk that the vegetables will contain enough contamination to affect those who eat them. There was some anxiety during the last dry spell that not enough rain had fallen to wash away the toxic effects of such compounds. It is probable that symptoms of poisoning which occurred in Essex about two or three years ago were a result of contamination with organic phosphorous sprays, although luckily there were no fatalities. The great toxicity of insecticides was emphasized recently by the contamination of a railway waggon in Wales as a result of diendrine having leaked from a drum: this waggon was subsequently used to carry flour to a town in Wales. Flour was then baked into bread and distributed throughout the town and within a few hours of eating the bread over one hundred people were ill with coma, epileptic fits, drowsiness and vomiting. The contamination of the flour was extremely small which showed the excessive toxicity of this substance. Luckily there were no fatalities.

Other Poisons

While on the subject of flour, ergot poisoning of bread as a result of impure flour and its contamination by a toxic fungus produced several deaths in a French town with severe mental illness, about three years ago. No cases of ergot poisoning have occurred from this source in this country for the last twenty years.

Mellanby[5] has found that cases of epileptic fits in dogs were definitely associated with the eating of white bread which had been bleached by the addition of agene and it was thought that epilepsy might be produced in human beings in a similar way. All experiments, however, have failed to incriminate agenized flour as producing epilepsy in man or in other animals, and it would seem that the dog is peculiarly susceptible to this compound.

Before leaving organic compounds, mention should be made of carbon tetrachloride. This poison can produce some damage to the nervous system, but usually produces severe renal and liver damage. It is present, of course, in many proprietary compounds used in cleaning clothes and it is only dangerous if used in an enclosed space where the persons may absorb the fumes. For example two naval ratings working in a submarine, were poisoned as a result of cleaning their uniforms in an enclosed space without adequate ventilation.

The importance of the toxicity of the orthocresol derivatives has been emphasized recently once again. Several outbreaks of motor polyneuritis have followed the accidental contamination of food by these highly toxic derivatives. Ginger wine became

contaminated in the United States, margarine in Germany after the last war and a few cases of poisoning also occurred in Liverpool. Recently, however, a major outbreak in Morocco has occurred where it is estimated that probably 10,000 people were poisoned by the contamination of olive oil, used in cooking, by surplus jet fuel oil which was mixed with the vegetable oil and sold on the market by some ingenious Arab profiteers. The epidemic reached such proportions that the Moroccan Government asked for help from the World Health Organization and it became clear after investigation that only certain Arabs, using the poorer qualities of cooking oil, had become affected by the oil which appears to have a selective effect on the motor nerve, and to a lesser degree on the spinal cord. Luckily most cases recovered. Any outbreak of multiple paralysis of this kind should be suspected of being due to a poison, possibly orthocresol.

An interesting epidemic of epilepsy in babies in the United States was found to be due to the fact that a certain proprietary dried milk had been overheated with the result that the essential vitamin, pyrodoxine, had been destroyed; and as pyrodoxine is necessary for the development of the nervous system, epilepsy had resulted in these babies fed on this compound, due to a deficiency syndrome.

Whether we shall suffer any ill effects from the use of detergents, which is the other major change in domestic practice, no-one can say. All I know is that I heard of an M.O.H. who, when he washed up, always insisted that the china was washed in hot water after the use of detergents. He himself, however, has recently died of a carcinoma of the bronchus, possibly related to the fact that he was a heavy smoker. Detergents do not appear to be toxic to animals, except when they are put directly into the spinal fluid.

Infections from Pets

Having spent some time on chemicals I would now like to turn to pets in the home. There seems to be a myth in the lay minds that animal diseases are not transferable to man. One of the most serious groups of disease that has been transmitted to many by animals is due to leptospiral infections. A common variety is contracted from rats, either by bathing in water which is rat-infested or through abrasions caused by working in conditions where rats abound. Cases have occurred in Bristol from swimming in local streams and even from swimming in the Henleaze swimming pool. Certain industrial workers have contracted the disease, particularly fish workers in Aberdeen and miners in South Wales. The most unusual case which occurred was an epileptic who fell, after a fit, into a small pool of water and absorbed the infected organisms as a result of being immersed in water which must have previously had rat contacts. Another variety of leptospirosis is carried by dogs and about 20 per cent of the canine population of a large city appear to be infected[6]. The dog infection is also contracted by bathing and one patient acquired it through bathing in a pool in which a dead dog was later found. A commoner source of infection is by contamination of the skin with dog's urine which contains the organisms. A husband and wife living in Bristol both contracted a meningitis by this method of infection. Both types are commoner in the summer months, probably due to bathing.

Infection of human beings with psittacosis from budgerigars and parrots is not as common as it was, but cases producing an atypical pneumonia still crop up from time to time. Recently there has been some controversy over whether budgerigars carry poliomyelitis. It has always been suggested that poliomyelitis virus has an animal reservoir which may possibly spread the disease from place to place and the finding of a virus in a budgerigar was an interesting isolated observation which has not been confirmed.

Equine encephalitis is a disease which is confined to the United States of America but undoubtedly in this condition the virus is spread by birds for many miles and the bird does not apparently suffer any ill effects.

Dogs have been proved to be carriers of human tuberculosis, and Swedish workers have shown quite clearly that one dog infected six members of a family with tuberculosis, its original master died from the disease and the dog was looked after by another family who immediately contracted tuberculosis.

I have been interested in the possibility of cats being associated with polyneuritis of an infective type[7] and the scratch of a cat produces cat scratch fever with enlargement of the glands and skin lesions. Mice are also responsible for lymphocytic meningitis where food has been contaminated by mice.

A protozoal disease of animals, known as toxoplasmosis, has also been shown to infect man, and the disease has many symptoms including cerebral complications, eye lesions and glandular enlargement. It is probable that this disease is very prevalent in the animal kingdom, particularly in dogs, cats, rabbits and even in birds. From positive agglutination and complement fixation tests done on the population of cities, it is estimated that between 30–50 per cent of people are infected at some time in their lives without its producing any serious symptoms, but about one in five hundred people may get serious trouble. It is obvious, therefore, from these facts that children should not allow animals to lick their faces, that care should be taken not to allow animal excretion to contaminate open sores or utensils and that plates used by dogs should not be used by humans without adequate sterilization.

Neuritis from Compression

The housewife during the course of her duties is particularly prone to suffer from neuritis, owing to the irritation of peripheral nerves. It was pointed out by Walsh[8] that neuritis occurred in middle aged women mainly owing to repeated domestic duties involving lifting, washing, polishing, vacuum cleaning, etc., and he suggested that the tone of the shoulder group of muscles deteriorates. When the shoulder drops there is too little room for the outlet for the nerves forming the brachial plexus and as a result, particularly at night, these nerves are irritated and the patient gets painful neuritis down the arm. It is notorious that these symptoms are worse on waking, and pass off during the day; they are directly related to the amount of work done during the previous day, and the patient tends to lose his symptoms on holiday. Concentration, however, on this shoulder girdle syndrome had led to the neglect of the importance of wrist compression of the median and ulnar nerves, but in particular the median nerve, where it lies in the carpal tunnel and where particular movements of flexion with the wrist in hyper-extension, such as the classical example of hand milking, is apt to produce compression and irritation of the median nerve in the carpal tunnel. The carpal tunnel syndrome of median weakness and irritation is now common as a cause of pain in the arm and particularly the hand, and a great deal has been done by operations to relieve these sufferers. The diagnosis can usually be established by the typical median distribution of the sensory loss and the wasting of the appropriate thenar eminence. The superficial branch of the ulnar nerve can also be compressed at the wrist producing a motor weakness and often no sensory loss, and the ulnar nerve can also be compressed as a result of leaning on the elbows, such as the medical student indulging in excessive study, particularly if the nerve lies superficially in the groove at the back of the elbow. It is important if possible, to find out the particular pressure or movements which produced irritation of these nerves and one patient I have seen undoubtedly produced his ulnar paralysis by his method of sleep. He slept with his arm tucked underneath his head producing an ulnar nerve compression. This was so firm a conditioned reflex that his arm had to be put in plaster to prevent his adopting this posture unknowingly. As a result of this treatment his ulnar nerve paralysis cleared up completely. People are sometimes apt to get compression of the radial nerve from the use of crutches and a more unusual method of compression is from another human body compressing the arm against a hard surface, such as the back of a

cinema seat or the ground. This results in a drop wrist, which can be somewhat embarrassing to both parties; the compression may be as short as two hours and the recovery as long as six weeks. There are other forms of pressure neuritis which I need not deal with and are less common, but a careful history of what the patient does is essential to establish the correct diagnosis and appropriate prevention and treatment

In conclusion, I have tried to link together various forms of possible neurological hazard which are very diverse in their aetiology, but the majority of them occur in the home and may be of some interest to stimulate observation of other conditions of a similar nature. It is of interest that a large number of the conditions I have described have only been recognized within the last twenty years.

REFERENCES

[1] Hunter, D. and Russell, D. S. (1954). *J. Neurol. Psychiat.*, **17**, 235.
[2] Baker, *Med. Tr. Coll. Phy.* (London, 1772), **1**, pp. 175.
[3] McAlpine, D. (1959). Personal Communication.
[4] Campbell, A. M. G. (1949). *Lancet*, **2**, 1178.
[5] Mellanby, E. (1931). *Brain*, **54**, 247.
[6] Campbell, A. M. G., Macrae, J., Manderson, W. G., Sumner, K. C. and Broom, J. C. (1950). *Brit. Med. J.*, **1**, 336.
[7] Campbell, A. M. G. (1958). *Proc. R. Soc. Med.*, **51**, 157.
[8] Walshe, F. M. R., Jackson, H. and Wyburn-Mason, R. (1945). *Brain*, **67**, 141.

IGNAZ PHILIPP SEMMELWEIS AND HIS TIMES*

BY

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I have chosen Ignaz Philipp Semmelweiss as the subject tonight for two reasons. First, I have found that the name of Semmelweis is not very well known and I hope to show that it is a name worthy to be remembered, and secondly he belonged to the so-called Second Viennese School which once was famous all over Europe, and I thought you might be interested to glimpse at those times.

Let us go back to the end of the eighteenth century when considerable changes were made in the life of the Austrian people, especially under the Emperor Josef II (1780–90). He introduced compulsory education from six to thirteen, abolished serfdom (1789) and restricted the power of the Church, abrogating many clerical privileges and closing certain monasteries particularly those of the Jesuits. Serfdom was restored by his brother Leopold who reigned only two years and was succeeded by his son Franz II, the last Holy Roman Emperor and the First Emperor of Austria. All the internal problems were, however, overshadowed by the wars with France, which began in 1792 and lasted with interruptions until 1814. These brought to Austria a series of disasters: Austria lost her possessions in Italy and the Rhineland, Vienna was twice occupied by French armies and in 1806 Napoleon himself became universal Emperor. The prevailing instability made Franz II extremely conservative; he resisted change, popular initiative or indeed any movement in political affairs; his resistance to change was such that he would not even alter the reforms made by Josef II, although he wholeheartedly disagreed with all reforms introduced by his predecessor. When Franz died in 1835 he was succeeded by his son Ferdinand almost an imbecile.

In this unstable and rather confused atmosphere a very powerful Civil Service and Administration developed. Its head was the very able statesman Prince Clemens Wenzel Metternich, who had the complete confidence of the Emperor and the court in a wider sense. The many rules and regulations were exactly recorded and codified and the saying was:

"Quod non est in actis, non est in mundo".

Even the University came under control of the Ministry and this affected the academic Senate and the professors directly.

A professor regius ordinarius once confirmed by the Emperor was all-powerful in his own department and could not be removed unless he was offered a chair at another University.

Yet with this rigid imperial system the social life of Vienna offered a very different picture. Here were living or had recently lived Mozart, Haydn, Schubert and Beethoven and a circle of artists that included the painter Moritz Schwind, the poet Bauernfeld and Grillparzer, the singer Vogl and many outstanding musicians, among them the violinist Kreutzer to whom Beethoven dedicated the Kreutzer Sonata. If the regime was dour and gloomy, the population was gay and cheerful. Indeed, one can say that this ironic mixture persisted in Vienna until the end of the Empire. It was in contrast to that in Germany. The contrast was summarized at the end of the First World War when the people in Berlin said: "the situation is serious but not hopeless" and those in Vienna said: "the situation is quite hopeless but not serious".

*From an Address to the Bath Clinical Society, 13th February, 1959.

The hospital which was the scene of the work and suffering of Semmelweiss was the Lying-in Division of the General Hospital of Vienna. It had been founded by the Empress Maria Theresia in gratitude to Van Swieten, her Dutch doctor and founder of the greatness of the Viennese Medical School. The lying-in Division was found necessary because of the immense number of illegitimate children. This in turn was caused by a ridiculous law that forbad marriage to illiterates. Nor did this affect only the poorer classes for even among the well to do, the number of illiterates was considerable. The arrangements for admission to the Lying-in Division shed a sombre light on the state of society

The early figures of the Viennese School are an impressive line. After Van Swieten and Auenbrugger, who in the eighteenth century introduced percussion as a means of diagnosis and prognosis came the pathologist Johannes Wagner, a Bohemian by birth; he was one of the first who drew his conclusions from the changes in the affected organs and not from the symptoms alone. His personality drew men like Rokitansky, Kolletschka, Schuh ahd Skoda to Vienna. He died at 33 years of T.B. He was soon succeeded by Rokitansky of Koeniggraetz in Bohemia.

Rokitansky started medical study in Prague in 1822, where the young Purkinje was one of his teachers, but he went to Vienna in 1824 and graduated there in 1829. He became an unpaid assistant to Wagner whom he succeeded, first as professor extraordinarius, and in 1844 as ordinarius. Rokitansky is well remembered as the most widely experienced of all morbid anatomists; his series of post-mortems in 1829 begins with the number, 4,781 when he retired in 1875 (31st August) the serial number is 64,571. In addition to these he made 25,000 forensic medical post-mortems. It needed a great working capacity to sort out and adequately to present this enormous material.

Rokitansky's teaching then was that the great variety of diseases could be explained by a great variety of the mixture of the blood (Humoral pathology). These views were quickly set aside when Virchow's Cellular-pathology (*Omnis cellula, e cellula*) became known. Rokitansky had to work in two small rooms which could neither be heated nor ventilated. There wasn't even enough light and to see properly it was necessary to climb on to a chair placed on a table near the window. Not until 1862 that a new building was completed and over its door was fixed a quotation from Morgagni: *Indagandis sedibus et causis morborum*" ("For investigating of the seats and causes of diseases").

Rokitansky never practised medicine himself, but he made himself available when in 1831 and again in 1832 a severe epidemic of cholera of which more than 5,000 people died in Vienna. In politics he was a liberal, in those days considered outrageous, but nevertheless he was created a Counsellor (Hofrat,) a baron and a member of the *Herrenhaus* (House of Lords). He died three years after his retirement on the 23rd July, 1878.

The second Viennese School was completed by two great personalities, Skoda, and a little later, Hebra. Skoda was born in 1805 in Pilsen, again in Bohemia, the son of a locksmith. He began to study medicine at Vienna University in 1825, where, like his friend Rokitansky, he had to support himself by coaching younger students. He took his degree in 1831 and became an unpaid assistant at the General Hospital in 1832. In 1833 he became a paid assistant and so remained until 1839. In 1840 he became Head of the Department for Chest Diseases.

Medicine in general was then much under the influence of the philosophy of the time and might have so remained but for Skoda and those around him. We may recall Hahnemann's homoeopathic doctrine: (1755–1842) *Similia similibus curantur*, a dictum very fashionable in those days. Skoda's new findings developing the work of Auenbragger and were publicized by Franz Schuh. They were treated by his contemporaries with derision. It was a gibe of a professor von Hildebrand "I am fond of music, but have never heard a pneumonia play the fiddle". When Skoda retired in 1871 he said:

"now it is up to the microscope and chemistry". Skoda's aim was to concentrate on the physical methods of examination in diagnosis, a prognosis.

Ferdinand Hebra was an assistant of Skoda. He showed great interest in the diseases of the skin. At that time all sub-departments or, as we now call them, specialities, came under the supervision of the professor of general medicine. Skoda offered Hebra the opportunity to take over the care and supervision of the skin case of his department and thus Hebra became one of the founders of Dermatology. Prominent among Hebra's pupils were Kaposi and Philip Josef Pick. Hebra linked dermatology to Pathology, influenced by Rokitansky and his first paper was on scabies. Among other personalities of the Second Vienna School we may recall the anatomist Hyrtl, the physiologist Bruegge, the physician Oppolzer, the surgeons Schuh and Dummreicher, followed later by the eye specialist Arlt and the greatest of all, Billroth.

Contrasted with these pioneers was Johann Klein, professor of obstetrics, he was a narrow minded official, obedient to his superiors but impatient with his subordinates, unintelligent but very powerful, because he was not only regius professor and therefore irremovable, but also director of the General Hospital with its entire administration in his hands. No changes were possible without his consent, every detail had to come before him and was decided by him. Not only had he the final say in dealing with hospital problems as such, but he also could transfer, admit or dismiss both lay and medical staff. Thus, for example, he transferred Skoda before he became professor, from the General to a Mental Hospital in one of the suburbs because he disagreed with Skoda's use of the stethoscope. Only when Skoda's views were recognized not only in Vienna but also further afield was Klein forced to recall Skoda. We shall meet again the ill-famed Klein.

These were the men whom Semmelweis found when he came as a student to Vienna in 1837. He was born in Budapest on the 1st of July, 1818, the son of a shopkeeper. When he came to Vienna he was looked on by the citizens as an alien from an unfriendly land for the awakening of nationalism had begun to cause tension with Hungarians who sought independence. Semmelweis, a rather poor student, found himself lost and lonely in a strange and unfriendly world. For a few months he studied law; then changed to medicine. Rokitansky accidentally became aware of the poor and undernourished looking young man and invited him to stay at his house. After a break of several months in Budapest, owing to the death of his mother, Semmelweis returned to Vienna and, after qualifying, became assistant at the obstetrical clinic.

The obstetric clinic was divided into two parts, one was used for the training of medical students and was under the immediate direction of Klein, while the other was used for the instruction of midwives and was in charge of Bartsch. Semmelweis was at once shocked by the enormous proportion of deaths in Klein's clinic, amounting to 10 per cent. at least, sometimes rising to 20 per cent., while the number of deaths occurring on the second clinic was much smaller, fluctuated between 3 per cent and 4 per cent. The authorities, who considered puerperal fever as a peculiar form of epidemic disease, blamed all sorts of atmospheric, telluric, cosmic, and miasmatic influences for the mortality in Klein's clinic. Again they made overcrowding responsible and it was even said that the sense of modesty was too frequently violated because the male students came to examine the women. In the end foreign students were blamed and it was maintained that they were rough with the patients before and while they were in labour. This latter accusation went so far that the number of foreign students was restricted and when there ensued no reduction in the number of deaths, foreign students were excluded from Klein's clinic.

This state of affairs became of course known among the people and the women tried to avoid the first clinic. The two clinics admitted on alternate days and there was very often a fight not to be admitted to the "Death House" as it came to be named. Semmelweis writes: "One could see heart-rending scenes when patients on their knees asked weeping, to be discharged again after they found themselves by mistake in the first

clinic while they had expected to be or had booked for the second. Women in childbed with an uncountable pulse rate, enormous meteorism, dry tongue, gravely ill with puerperal fever declared only a few hours before their death that they were quite all right, to avoid treatment, which they knew was but the fore-runner of death". Semmelweis was desperate and could find no explanation for the enormous proportion of deaths in the first clinic while that in the second clinic remained around 3 to 4 per cent. The findings of the Royal Commission, which had blamed the foreigners, bad ventilation, dirty linen etc., in 1846 were to him not a sufficient explanation. He noticed, however, that all women who had been in labour with a slow first stage were taken ill during the 24–36 hours after delivery and died very quickly and that the children also died soon afterwards. Yet a woman who was delivered in the street had a much lower morbidity—and mortality rate.

In complete helplessness Semmelweis abolished the posterior position in labour used in the first clinic and introduced the lateral position just because it was practised in the second. Still the mortality rates remained the same. Depressed and exhausted, he went in the early spring of 1847 to Venice to forget the horrors at the clinic. When he returned after three weeks to Vienna he heard to his dismay that his friend Professor Kolletschka had died. Kolletschka had been doing most of the post mortems in connection with forensic medicine and, while performing a post-mortem, cut his finger. An infection set in with severe lymphangitis and lymphadenitis and death occurred within a few days. The findings at the post-mortem were: bilateral pleurisy, pericarditis, peritonitis, meningitis, metastases in one eye—very much as he had seen in so many of his patients who had died of puerperal fever.

It now became clear to Semmelweis that there must be a direct connection between the death of Kolletschka and the deaths of hundreds of his patients, in fact, that he had died of puerperal fever. The medical students coming from doing post-mortems under supervision of the Professor or his assistants, and then coming directly to the Lying-in Division and examining the women in labour, *must be the carriers* of some sort of poison which was causing the puerperal fever. He came to the conclusion that particles from a corpse, were adherent to the fingers of the students or the doctors passing directly from post-mortem room to the women in labour and there examining patients without properly washing their hands. It was, he believed, their fingers that were responsible for the introduction of the material which carried the fever that killed his patients.

To prove the correctness of this view Semmelweis, in 1847, made it a rule that all students and doctors must wash their hands first with soap and water and then in a solution of Calcium Chlorate before examining patients. The immediate result was a startling change in the mortality rate of the first clinic. From more than 12 per cent. it sank, to the same level as that of the second clinic.

In October 1847, a patient in labour and suffering from a carcinoma of the uterus was admitted to bed number one where the round always started. After she had been examined, the students and doctors washed their hands but with soap and water only and of 12 women who were delivered at the same time, 11 died of puerperal fever. This was for Semmelweis proof enough, that not only disentegrating organic material from a corpse but putrefying organic material from the living is capable of producing puerperal fever. Soon after there was a like experience with a woman suffering from a septic knee, and his views were reinforced.

Just at this time Professor Klein, who seems to have disliked Semmelweis from the beginning, began to make difficulties, which in the end forced Semmelweis to leave Vienna. Without giving any reason he ridiculed Semmelweis before the medical students by pointing out that Semmelweis' views were not sufficiently tested; and he gave orders that no further Calcium Chlorate should be supplied to the wards, as the cost was too high. As a matter of fact it was very cheap, and, as Semmelweis was determined to use it, he provided the necessary money himself.

But Klein was not beaten; he now told the students that the ideas of Semmelweis

were useless, and that he had no objection if the orders of Semmelweis on washing were not observed. Meantime, the views of Semmelweis had been favourably mentioned in two articles by Hebra in a Viennese journal (December 1847 and April 1848) and Haller, one of the physicians also spoke of Semmelweis's success in a lecture and expressed himself favourably concerning the practical consequences of Semmelweis's doctrine. The first full exposition was that of Skoda in a lecture delivered in the Viennese Royal Academy in 1849. In May 1850 Semmelweis himself developed his views on the cause of puerperal fever and rejected the idea of direct contagion. Not every patient suffering from puerperal fever will transmit the condition to a healthy person, and on the other hand, a healthy person can become infected with puerperal fever from a person who herself is not suffering from the disease. As a comparison he says: "every person suffering from small-pox is capable of transferring the illness to a healthy person, and a healthy person can only be affected with the same disease by a person suffering from smallpox. No person will become infected with smallpox from a person suffering from a carcinoma of the uterus. When puerperal fever takes its course under conditions where no organic material disintegrates or putrefies, then puerperal fever is not transferable to a healthy person. If on the other hand disintegrating organic material is produced in the course of puerperal fever, as for instance a septic endometritis, then puerperal fever is transferable to a healthy person. After death it is transferable from any corpse, but then it is the degree of decomposition which matters. Puerperal fever may originate from diseases which by themselves are not puerperal fever, for instance erysipelas, carcinoma of the uterus, etc. Therefore, he concludes, puerperal fever is not a contagious disease, but it is transferable to a healthy person by decomposing organic matter. Such a transfer can start anywhere outside or inside the human body where continuity of the normal integument, epidermis or epithelium is broken.

It should here be recalled that along with the high mortality rate of the mother at Klein's clinic was the perhaps still higher death rate of the new-born, who after the mothers' deaths were transferred to a foundling asylum. There too the post-mortem findings were identical with those of their mothers: Bednar, the physician to the asylum reported in 1850: "septicaemia in the newborn has now become very rare and for that we have to thank the discovery of Semmelweis who found the cause and means of prevention of this murderous disease". Most Continental obstetricians and pathologists still believed that a *genius epidemicus, i.e.* a cosmic or telluric miasma caused puerperal fever and the doctrine of Semmelweis was rejected by most. Their view was rigorously expressed in 1858 by the Academy of Medicine in Paris and in 1861 by the "Versammlung deutscher Naturforscher" (Congress of German Scientists) at Speyer. Dubois in Paris, one of the highest medical authorities in France said in 1858: "The views of Semmelweis generally accepted in Germany and England, that the transmission of puerperal fever may take place by the blood, by various discharges from the diseased or by decomposing organic material, has been proved wrong, and perhaps this doctrine is by now completely forgotten at the place where it originated. But of course that does not mean that one should not be careful and take all precautionary measures but I do not think that all the contagious qualities are either so constant or so persistent or vigorous as was alleged in the reports. If it were really so serious, the whole staff of the hospitals would have to be kept in strict quarantine, otherwise the public would constantly be in great peril. Therefore it is due to the public to reduce the exaggerated assumptions to their proper level. In many women before delivery these are conditions which favour the development of puerperal fever, as can often be seen in private practice and in hospitals. In the latter many women, pregnant or in labour, arrive with evident symptoms of puerperal fever which very often takes a rapid course." Semmelweis answered "My teaching is slandered in Vienna but not forgotten."

Another opponent was the pathologist Virchow in Berlin who called Semmelweis a speculator and in 1858 still made the weather responsible for puerperal fever.

Semmelweis called him a bad pathologist. In 1863 Virchow was still saying "The main factor in the origin and the spread of puerperal fever is a predisposition of the individuum for the development of diffuse and malignant types of inflammation and therefore the development of puerperal fever can happen even without a contagium". And again "For many years while I have daily handled corpses and pathological specimens I have been at the same time, in my wards at the Charité, and have treated women in child-bed with the very best results".

The most violent opponents of Semmelweis were, however, his fellow gynaecologists. It would take several articles to quote all the opponents who made life for Semmelweis hard indeed. One of the most emphatic was Scanzoni, Professor of Obstetrics in Wurzburg, and previously in Prague and there developed a quarrel between the two which went on for years; Semmelweis called him "the Nero of Medicine".

Semmelweis continued to try very hard to convince his chief Klein, that the measures taken by him were effective and that other obstetricians in Vienna and Prague as well as in Germany, France and England were sending him favourable reports. The relationship between the two grew worse and in 1849 Semmelweis decided to resign his post and to ask for right of a free teacher at the University, which he hoped would be granted him with the help of his friends Skoda, Rokitansky and Hebra. But he reckoned without Klein, whose influence with the authorities was so strong that the request of Semmelweis was bluntly rejected without reason given. A year later he made a second application and this time it was granted but with the restriction that he was allowed to discuss only the *theory* of obstetrics and that no practical demonstration was allowed.

Tired and disappointed he left Vienna for Budapest in 1850. Soon after he met his colleagues at a discussion of the Budapest Medical Society and his theory was of course discussed and straightaway attacked. He was told that there was a serious outbreak of puerperal fever at the St. Rochus Hospital where there are no students to be blamed. When he went there the next day he found that the surgeon in charge of the hospital was not only looking after his surgical and gynaecological patients, but he was at the same time also pathologist of the place and he and his assistants did all the post mortems! In 1851, Semmelweis was appointed unpaid Honorary Primarius and chief of the gynaecological and obstetrical unit at the St. Rochus Hospital, a post he held until 1857. In 1855, after the death of Professor Birly, he was appointed to the chair and became professor ordinarius at the University. The condition of the buildings of the St. Rochus—and the University Hospital in Budapest were if possible even worse than in Vienna.

The remaining years of his life were spent in Budapest, where he tried hard to convince his colleagues and pupils of his views. He proded their truth by reducing the death rate of puerperal fever to a hitherto unknown low figure; yet he still met fierce opposition and he became a tired, exhausted man, often suffering from insomnia and taking refuge in hard work. At the end of 1864 a condition developed which for a time kept him from work. He recovered but, in 1865 it was found necessary to admit him to a private asylum in Dobling near Vienna, where Hebra had found a room for him. He died a few days later of a septicaemia from a small wound on his finger, acquired at an operation which he performed in one of his last lucid moments. The post-mortem findings (recorded on the death certificate) were exactly the same as those of the victims of puerperal fever. He was buried in Vienna. Thirty years later his body was brought to Budapest and buried there.

As we have seen, the situation on the Continent was as black as it could be before Semmelweis took up his fight against the mortal danger of childbed fever. The situation in England and in Ireland was very different. The main reason for this was: firstly that puerperal fever was regarded there as a contagious disease and strict precautions were taken to prevent its spread; and secondly, that long before Semmelweis

emitted his calls of warning the same ideas had been expressed there and led to the necessary precautions. These included the washing of the hands in antiseptic liquid. Charles White of Manchester in his *Treatise on the Management of Pregnant and Lying-in Women* (1773) asked that special attention should be devoted to all such matters as good hygienic surroundings, scrupulous cleanliness both personal on the part of all attendants and also of any material likely to come into contact with the patient, as bed linen, towels, sponges, instruments: proper ventilation of the labour room, maintenance of an even moderate room temperature and correct posture of the patient. As a result of his methods he reported that of the large number of lying-in patients he had delivered, he had never lost one from puerperal fever. Similar good results of White's methods were reported from Dublin. In 1841 Storrs of Sheffield, from his own observations and from evidence collected among his friends came to the conclusion that (1) puerperal fever may be communicated by touch and (2) that it originates in some animal poison, especially from erysipelas and its complications and in a lesser degree from typhoid fever. He therefore drew up the following rules for the obstetrician: (1) to avoid treating cases of erysipelas and (2) to avoid post-mortem examinations. If either or both of these procedures are unavoidable, then the practitioner should use disinfectants and change his clothes. Thus, disinfection measures against puerperal fever were already used in Great Britain and Ireland before Semmelweis' calls of warning.

Dr. Arneth, an assistant in the Viennese Obstetrical Clinic for midwives, a friend of Semmelweis and one of his earliest disciples, wrote in 1847 to the most famous obstetrician and gynaecologist of the time, James Young Simpson in Edinburgh and asked for his opinion. Simpson mistook the theory of Semmelweis for the English doctrine of contagion and was caustic in his reply. Later Simpson was made familiar with Semmelweis' views by Arneth in person and his reception was tolerant and dignified, while at the same time he put forward his own idea of the cause of puerperal fever. Simpson thought, that generally, if not always, the material which, when carried from one subject to another, could produce puerperal or surgical fever in a newly inoculable subject, was an *inflammatory secretion*, like the inoculable matter of small-pox, cow-pox, syphillis etc. Obstetricians had now a very decided proof of various kinds of morbid matters which were capable, when inoculated into the vagina of leading to puerperal fever. Simpson later abandoned the opinion that puerperal fever is a specific contagious disease and considered it to be identical with surgical fever. "The fever" he says, "is not the cause of the accompanying inflammation but the fever as well as the inflammations are the result of a common cause, namely the original corruptions of the blood. But what causes the corruption of the blood must be answered in a later era with a more developed pathological anatomy, histology and chemistry". Semmelweis answered Simpson by saying: "By Pyaemia I understand a disintegration of the blood, brought about by the introduction of a decomposed animal-organic matter and I call puerperal fever a variety of pyaemia".

We see the confusion that reigned in those days, when almost everybody anticipated the true essence of infection and yet: nobody knew.

Semmelweis was not a great writer. He published few papers, but in 1861 appeared his book: *The aetiology, conception and prophylaxis of puerperal fever*. In 1884 a textbook of gynaecology was published by Fritsch, then professor of gynaecology and obstetrics in Breslau; he referred to Semmelweis in these words: "In the history of midwifery there is a dark page, and it is headed: *Semmelweis*. What man could close his eyes to the powerful impression of his book? Even now there are whole pages of his deductions which might stand in the most modern work. And the annihilating logic of his statistics! We younger men, for whom antipathies are unthinkable, to whom the reading of coarse tirades about "genius misunderstood" are merely tedius, often find it incomprehensible that the logical conclusions to the doctrine infection were nowhere

drawn: I refer to the local treatment. The efficient application of disinfection in midwifery is without doubt due to surgery yet most certainly it should have been the reverse. If the councils of Semmelweis had been followed, the truth of his doctrine would have been demonstrated in the compelling language of statistics, and so perhaps obstetrics would have stood in the forefront of the greatest advance in medicine of all time".

Semmelweis was not first to realize the devastations caused by puerperal fever, but none of his predecessors nor contemporaries had posed the problem of puerperal sepsis as clearly as he, for Semmelweis this was not only the fulfillment of his professional duties; it was a mission. Two discoveries at the beginning of this era of medicine had been of the highest importance in saving of life and preventing suffering: the discovery of Edward Jenner and that of Ignaz Semmelweis. In neither case did the discovery fall from heaven; in neither case was there a grasping of Promethean fire; for neither can one speak of inspiration. The discovery of Semmelweis was possible only for one who had prolonged and laborious preparation, who had directly observed and had reflected without preconceptions, whose intellect was alert and keen by reason of his human sympathy. The magnitude of his service to mankind on the one hand and his sufferings from jealousy, ignorance and ingratitude from his contemporaries on the other hand were extraordinary. The methods used against him to belittle and to destroy him were of a unique variety, intensity and extensiveness. When I have sometimes asked people whether they know or have heard of the name of Semmelweis the answer has been "Oh yes, but I cannot remember what he was or did"; or not infrequently "Never heard of him"!

But I am sure many of you will agree that he deserves to be remembered as one of the great personalities of the guild of Hippocrates.

"RENAL COMPLICATIONS OF DIABETES MELLITUS"

A Clinical Pathological Conference of the University of Bristol Medical School
(*P.M.* 6169)

CHAIRMAN: PROFESSOR T. F. HEWER

Professor Hewer: I will ask Dr. J. E. Cates to give us the clinical history of this patient.

Dr. J. E. Cates: Miss L. W. aged 55, a known diabetic, was admitted to Bristol Royal Infirmary on the 11th May, 1959, and died in uraemia three days later. Diabetes was diagnosed first in 1951 shortly after the death of her mother. We have no details of her treatment at that time, except that she was not given insulin. She first came to the Bristol Royal Infirmary as an out-patient in May 1955, referred by her family doctor with the diagnosis of diabetes, and with a report that her urine contained a trace of sugar, much albumin and some pus. The doctor also reported that whereas six years ago her blood pressure was 165/90 it had risen now to 205/105. Apart from the usual symptoms of diabetes, she complained of ankle swelling and shortness of breath. She was very fat and was therefore given a low calorie diet which caused her to lose 14 lb. in weight; her urine became sugar-free, and her blood sugar fell to normal levels. Her urinary infection was due to *Bacillus coli* which was sensitive to sulphonamides, tetracycyline, chloramphenicol and streptomycin; and granular casts were also noted in her urine. She was given a course of sulphonamides. The urinary infection was not eradicated and she defaulted from the clinic. She also had early cataracts, and was referred to Bristol Eye Hospital for opinion.

Three years later (September 1958), she was referred to the Diabetic Clinic from the Eye Hospital because her diabetes was not fully controlled. She was now complaining of increasing breathlessness, orthopnea, and some chest pain on exertion. She was still very fat, her blood pressure had now risen to 260/140 with an increase in her heart size and a palpable gallop rhythm. There was ankle oedema and râles at her bases. There was also diabetic neuropathy with absent ankle jerks and reduced sensitivity to pin prick below the knee. In her fundi there were excessive haemorrhages and exudates, and a blurring of her disc margins. The urine still contained much albumin, pus and a heavy growth of *Bacillus coli*. Her blood urea was now raised (100 mg. per cent). There was very little glycosuria; and her blood sugar was 160 mg. per cent two hours after food. Her practitioner was again asked to prescribe a course of sulphonamides but advised not to give potassium citrate. She attended at fortnightly intervals and was prescribed a low calorie diet on which she lost weight, and her blood urea rose to 122 mg. per cent. She was advised to come into hospital for more vigorous treatment of her urinary infection but declined and once more defaulted.

In May 1959 she was admitted as an emergency with a three-day history of passing no urine at all. Two weeks before this she had felt unwell, nauseated and had vomited once or twice. Her skin had begun to itch and for the first time she had burning and smarting on micturition, with a little blood in her urine. At the same time she had a sore throat, and reported that her doctor had given her tablets.

On examination she was now grossly oedematous, and was overbreathing. Her breath smelt uraemic and foul. Her mouth contained stale blood from her bleeding gums. The other physical findings were as before, except that her blood pressure had fallen to 145/70; blood sugar 160 mg. per cent. Throat swab showed no growth of haemolytic streptococci. Blood N.P.N. 246 mg. per cent; sodium 128 m. eq.; potassium 6·3 m. eq. Catheterization of her bladder yielded no urine. The next day Mr. Ashton Miller catheterized her right ureter and found no obstruction up to 25 cm.;

the left ureteric orifice was not seen. On the 13th May N.P.N. 326, K. 7·4 m. eq. alkali reserve 8 m. eq. She was treated with intravenous tetracycline and penicillin and was given resonium by stomach tube together with glucose. She died in coma the next day.

We felt that this lady had chronic pyelonephritis, probably with an acute flare-up of recent onset, over the previous two weeks; the heavy albuminuria throughout suggested that her kidneys were probably affected by the diabetic glomerulo-sclerosis described by Kimmelstiel and Wilson.

There were two other probabilities that needed excluding: one was that she might have developed papillitis necroticans and that a papilla might have sloughed off and blocked her ureter. Mr. Ashton Miller helped to exclude this by his ureteric catheterization. The second possibility was that her family doctor had given her sulphonamide again and that she had developed anuria from this, but we learned soon after admission that he had prescribed hydrochlorthiazide and Rauwiloid.

Question: Was an artificial kidney available and would this have been a valuable treatment ?

Dr. Cates: No, it was not available. Even if it had been, I should not have used it because all the evidence indicated that this woman's kidneys were permanently and severely damaged. An artificial kidney is of value for tiding people over a period of temporary renal insufficiency.

Question: What are your criteria for deciding that a kidney lesion is irreversible ?

Dr. Cates: From the history of her slowly developing impairment of renal function, and from our failure to find a reversible condition.

Question: How was it that the blood pressure fell ? Could this have aggravated her renal failure ?

Dr. Cates: It is certainly true that a fall in blood pressure might have decreased glomerular filtration. We did not discover a separate cause for this fall in blood pressure; blood pressure often falls in the closing stages of uraemia.

Question: Would Dr. Cates like to comment on the value of sulphonamide in the treatment of pyelonephritis ?

Dr. Cates: The weight of evidence is that sulphonamides are not likely to eradicate the infection within the kidney substance in pyelonepritis; for some years now I have preferred to give large doses of antibiotics for ten days or more at a time, almost on the scale of that needed in B. coli endocarditis.

Question: Would Dr. Cates condemn the use of sulphonamides in all cases of urinary infection ?

Dr. Cates: Oh no. In an acute cystitis, after catheterization for example, sulphonamides may be enough. But even then you ought to check the urine after a few weeks to see if it is still clear.

Dr. H. M. Leather: If the blood urea is high it is a safe rule not to use sulphonamides.

Dr. Cates: I agree.

Dr. W. O. Spence: Would Dr. Cates mind repeating what he said about the use of citrate in renal insufficiency ?

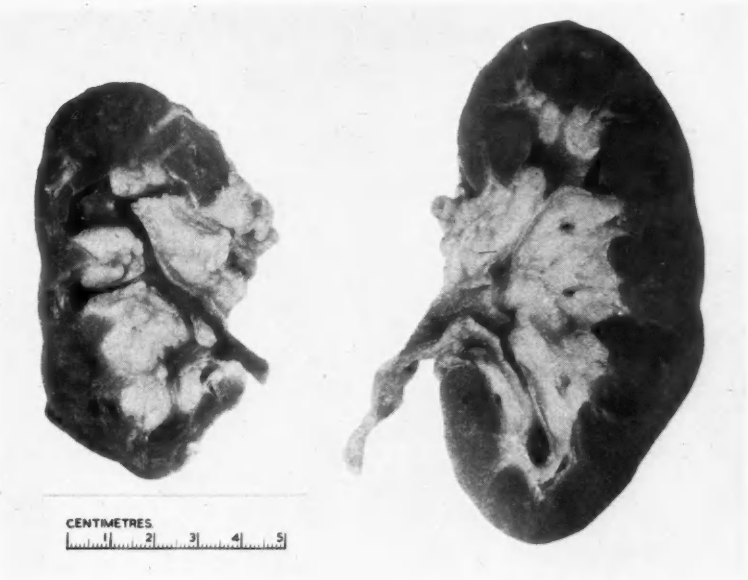
Dr. Cates: It is the potassium that is dangerous if renal function is impaired. The citrate radicle is innocuous.

Question: Did diabetic coma play any part in this woman's illness ?

Dr. Cates: No; though the obvious acidosis raised the possibility. But her blood sugar was normal and we couldn't detect ketones in her breath. In doubtful cases where there is no urine you can use a Rothera test on plasma.

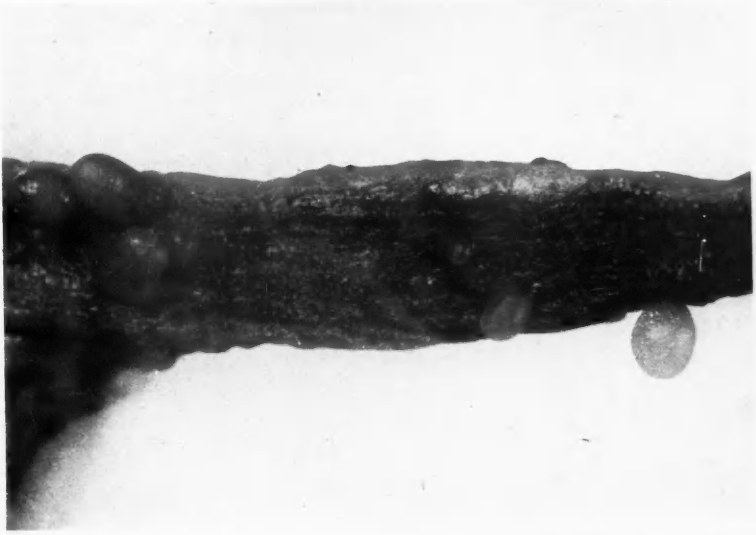
Professor Hewer: I think I probably ought to give the post mortem findings at this stage. This was a very obese woman who died with some oedema of the lungs and a bilateral pleural effusion. The heart, which weighed 585 grams, had considerable left ventricular hypertrophy and some hypertrophy of the right ventricle as a result, no doubt, of recurrent attacks of left ventricular insufficiency. There happened to be a

PLATE III



Kidneys.

PLATE IV

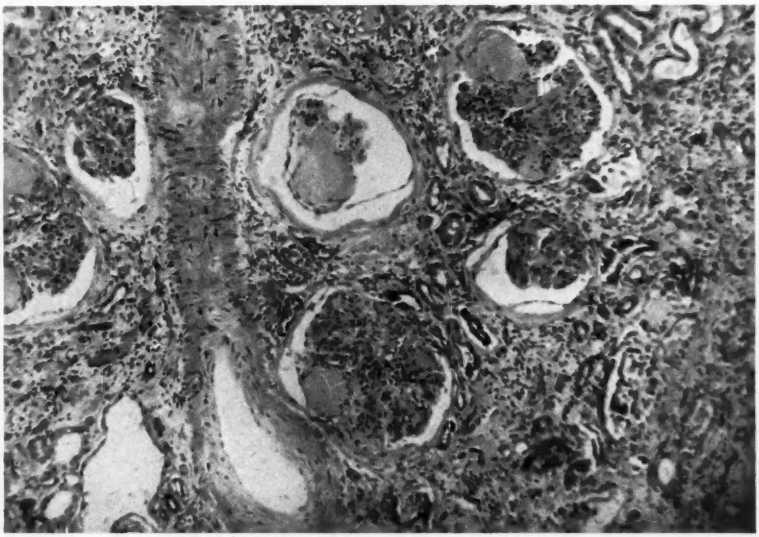


A segment of ureter showing several mucous cysts projecting into lumen. × 3.

PLATE V

Photomicrograph of section of ureter showing a small cyst and, on the left, a mucous gland becoming dilated. ×70.

PLATE VI



Kidney: glomeruli with some ischaemic shrinkage and large hyaline Kimmelstiel-Wilson lesions. ×75.

PLATE VII

Kidney: an arteriosclerotic interlobular artery with a narrow lumen due to intimal thickening; scarred and hyalinized glomeruli due to ischaemia, and dilated atrophi tubules full of hyaline casts. × 75.

congenitally bicuspid aortic valve but this had not contributed to her cardiac embarrassment and there was no other change in the heart. There was a good deal of atheroma in the aorta but the renal arteries in particular were very atheromatous and the branches to the right kidney were extremely narrow. As you will have gathered the kidneys were the most interesting part of the necropsy. The left kidney was much larger than the right weighing 220 grams while the right weighed only 115 (Plate III). This difference was due largely to a considerable shrinkage of the upper half of the right kidney as a result of extreme atheromatous narrowing of the branches of the renal artery supplying that area. In all other respects the two kidneys were identical, the capsule stripping with some difficulty leaving a granular surface. The general pattern of the left kidney on section was reasonably normal with diffuse scarring and just a little dilatation of the pelvis. The pelvis of each kidney showed a few small cysts projecting on the surface and these cysts were present throughout the length of both ureters (Plate IV), projecting like a series of minute balloons full of mucus. They must have caused quite appreciable obstruction to the flow of urine down the ureters. The condition is that of pyelitis cystica and ureteritis cystica. As will be seen in the photograph (Plate V) these cysts are due to dilatation, as a result of obstruction, of small mucous glands beneath the epithelium lining the ureters. This state of affairs is sometimes found in chronic inflammation of the urinary tract. It is occasionally present in the urinary bladder also but in this case there was only a mild subacute cystitis with no cystic change.

The microscopic appearance of these kidneys was quite remarkable. Several different conditions were present, all of them being quite frequent accompaniments of chronic diabetes. Firstly there was the condition of glomerulosclerosis of Kimmelstiel and Wilson. Nearly every glomerulus, in both kidneys, had in the substance of the glomerular tuft one or more round hyaline bodies which stained pink with eosin and gave a fine fibrillar staining with silver impregnation for reticulin (Plate VI). These lesions develop in the wall of the capillary vessels of the glomerulus. They contain little or no lipid. They undoubtedly give rise to a considerable reduction in blood flow through the glomerulus. Another change in all of the glomeruli was the presence of a quite uniform fibrous thickening of the walls of all the capillary loops in the glomeruli amounting to a diffuse glomerulosclerosis. A third manifestation of glomerular damage, which, like the Kimmelstiel-Wilson lesion, is pathognomonic of diabetes, was an exudative lesion at the periphery of the glomerulus consisting of a very acidophil vesicular lesion which, in frozen sections, contained anisotropic lipid. This is the exudative lesion which was described by Dr. G. F. M. Hall (1952) of this Department.

In addition to these glomerular lesions all of the afferent arterioles were very much thickened and completely hyalinized as a result of the hypertension. All of the branches of the renal artery within the kidney showed a considerable degree of narrowing as a result of intimal proliferation and atheroma. In the right kidney the area which was supplied by the very much narrowed renal arteries had shrunken as a result of ischaemia and it was interesting to see that the glomeruli in the ischaemic area were almost totally scarred but still showed signs of having had the Kimmelstiel-Wilson nodular lesions. This is interesting in that it is evidence that the Kimmelstiel-Wilson lesion appeared before the renal artery narrowing gave rise to such severe ischaemia.

In both kidneys there were some tubules containing polymorphonuclear leucocytes which can be interpreted as evidence of a slight pyelonephritis in an active stage. In the more scarred parts of both kidneys were numerous greatly atrophied renal tubules which were dilated and full of protein material giving them the appearance of thyroid tissue. This is rather characteristic of chronic pyelonephritis (Plate VII).

Another lesion of some interest in the kidney was the presence of some necrosis of the epithelium of the collecting tubules in the medulla together with a number of desquamated cells lying in the lumen. This necrosis of tubule epithelium is called lower nephron nephrosis and it is found in a variety of conditions where the renal blood

flow is drastically reduced. I think you will agree that there are plenty of reasons in this case for such a reduction of blood flow and when one remembers that the blood pressure of this patient fell considerably towards the end it is not surprising that lower nephron nephrosis occurred. By this time undoubtedly renal blood flow was so reduced that there was practically no glomerular filtration and this explains the anuria.

Mention has been made by Dr. Cates of the possibility of renal papillary necrosis as a contributory factor in causing the anuria in this case. Some of the calyces in the ischaemic part of the right kidney were dilated and it looked at first sight as though the tips of the pyramids had in fact disappeared, but careful histological examination showed no evidence of any old papillitis necroticans.

We can conclude, therefore, that these kidneys suffered from several conditions, all of which contributed to a reduction in the renal blood flow and glomerular filtration. There was a generalized glomerulosclerosis, with the nodular Kimmelstiel-Wilson lesions, an exudative type of glomerulosclerosis of diabetic origin, arteriolar sclerosis resulting from the hypertension, general renal artery narrowing produced by atherosclerosis, and some obstruction to the ureters by the condition of ureteritis cystica. There was also a mild pyelonephritis. Lastly one might mention tubular necrosis which may well have been due to the fall of blood pressure.

Changes in other organs were not of great significance. There was a generalized arteriolar hyalinization as a result of hypertension. The uterus contained numerous fibroids and some endometrial polyps. There were no obvious lesions in the islets of Langerhans.

It is quite clear that all the renal lesions that I have described were amply sufficient to account for the renal failure and I am sure that Dr. Cates was fully justified in considering that this woman's renal state was irrecoverable.

Question: Did you give the patient any insulin ?

Dr. Cates: No; she was a fat mild diabetic who readily responded to dietary restriction: she lost her glycosuria, and her blood sugars were virtually normal when on this regime. I am not certain, however, whether she ought not to have had a little insulin in view of her retinopathy. What does Dr. Mather think about that ?

Dr. H. G. Mather: I don't think insulin does make any difference in a case like this.

Professor Hewer: There is little more to be said about this patient. It is clear that she exemplified most of the renal lesions that occur in chronic diabetes.

REFERENCE

Hall, G. F. M. "The significance of atheroma of the renal arteries in Kimmelstiel-Wilson's Syndrome" *J. Path. & Bact.*, **64**, 103–120.

Notes and News

Professor A. V. Neale has been appointed Heath Clark Lecturer (University of London) for 1961.

Mr. J. H. Peacock gave an Arris and Gale Lecture at the Royal College of Surgeons on 22nd March.

Examination Results

UNIVERSITY OF BRISTOL

M.D.: T. J. Butler (with Distinction), C. C. Downie, J. E. Tovey.
Ph.D.: P. Radford.

M.B., Ch.B.

Aubee, R. I. A. A.	Mayne, Madeline, D.
Benson, J. A. G.	Randell, D. T. H.
Duff, G. C.	Sibbald, Dorothy M. I.
Haskins, H. W.	Stayte, D. J.
Heighton, D. R. M.	Ugwunze, M.
Hill, J. P. A.	Undugodage, R. J.
Hodge, R. C.	Davies, K. R.
Lockett, G. W. E.	Kerr, G.

Appointments

P. A. James, M.B.(BRISTOL), F.R.C.S., thoracic surgeon (specialist), Uganda.
R. A. Sharpe, M.B.(BRISTOL), M.O. Bahamas.

UNITED BRISTOL HOSPITALS
DECEMBER 1959 TO FEBRUARY 1960

Name	*Appointment*	*Formerly*
CATES, JOSEPH ELMHIRST, M.D., F.R.C.P.	Consultant Physician to the United Bristol Hospitals and the South Western Regional Hospital Board in the Bristol Clinical Area	Lecturer in Medicine, and Assistant Physician, United Bristol Hospitals.
GUPTA, P. B., M.B., B.S., F.R.C.S., M.CH.(ORTH.)	Senior Orthopaedic Registrar	Resident Orthopaedic Registrar, Norfolk and Norwich Group of Hospitals.
NESLING, A. E., M.B., CH.B.	Registrar in Anaesthetics	Registrar in Anaesthetics, City General Hospital Sheffield.
WALDRON, B. LE G., M.B., B.CH., D.A.	Registrar of Anaesthetics	Senior House Officer in Anaesthetics, United Bristol Hospitals.
WINSTONE, A., B.D.S., L.D.S.R.C.S.	Registrar in Dental Surgery	Dental Officer in the Royal Navy.

Mr. J. S. Cooper, B.D.S., has been accorded honorary status as Registrar in the United Bristol Hospitals during the tenure of his appointment as Lecturer in Dental Surgery to the University of Bristol.

SOUTH WESTERN REGIONAL HOSPITAL BOARD
DECEMBER, 1959 TO FEBRUARY, 1960

Name	*Appointment*	*Formerly*
	BRISTOL	
RODDIE, R. K., M.B., CH.B., B.A.O., F.R.C.S.	Consultant E.N.T. Surgeon, to the Bristol Clinical Area	Senior Registrar, E.N.T. Belfast Group of Hospitals.
FOSTER, G. S., M.D., B.S.(LOND.), M.R.C.O.G.	Consultant Obstetrician and Gynaecologist to the Weston-Super-Mare Group of Hospitals.	Senior Registrar in Obstretrics and Gynaecology, the United Cardiff Hospitals.
WILSON, F., M.B., B.S. (LOND.), F.F.A.R.C.S.,	Temporary appointment of Consultant Anaesthetist, Southmead Hospital, Bristol.	Senior Registrar and Lecturer in Anaesthesia, University of Liverpool.
	BATH	
COLLEY, J., B.SC.(LOND.), M.B., B.S.(LOND.)	Medical Registrar to the Bath Group of Hospitals.	Clinical Officer in Medicine, BMH, Cyprus (Captain R.A.M.C.)
	SOUTH SOMERSET	
LEIGH, H. I., M.B., CH.B.(BRISTOL), F.R.C.S. (EDIN.)	Re-appointed Surgical Registrar, Musgrove Park Hospital, Taunton.	Surgical Registrar, Musgrove Park Hospital.
	NORTH GLOUCESTERSHIRE	
CHAMBERS, R., M.B., B.S. (DURHAM), D.P.M.	Assistant Psychiatrist Horton Road and Coney Hill Group of Hospitals.	Senior Registrar, Newcastle General Hospital.
LEWIS, J. W., M.B., B.S.(LOND.), D.(OBST.) R.C.O.G.	Re-appointed Clinical Assistant in Gynaecology, Stroud General Hospital (1 session).	In General Practice in Nailsworth.
GOMPERTZ, R. M. H., M.B., B.S.(LOND.), D. (OBST.) R.C.O.G., D.C.H.	Clinical Assistant in Paediatrics, Cheltenham (4 weekly sessions).	Is in general practice in Cheltenham.
DUNBAR, P. G., M.B., B.S.(LOND.), D.A., D. (OBST.) R.C.O.G.	General Practitioner Anaesthetist, Devizes Hospital (1 session).	In general practice in Devizes.
	DEVON AND EXETER	
HATCHER, G. W., M.A. (OXON.), M.B., B.S., D.R.C.O.G.	Clinical Assistant in General Medicine, Tiverton and District Hospital, (3 sessions).	Junior partner in general practice in Tiverton.
COOPER, R.A., M.B., B.S. (LOND.)	Temporary General Practitioner Anaesthetist, Bideford Hospital. (half-days per week).	In General Practice in Bideford.
SOLAN, M.J., M.B., B.S. (LOND.)	Surgical Registrar, South Devon and East Cornwall Hospital, Plymouth.	
O'ROURKE, D. A., M.B., B.S.(AUST.), F.R.C.S. (EDIN. & ENG.)	Surgical Registrar, South Devon and East Cornwall Hospital, Plymouth.	Senior Surgical Registrar, Institute of Urology, St. Paul's.
BHONSLE, R. S., M.B., B.S.(BOMBAY)	E.N.T. Registrar South Devon and East Cornwall Hospital, Plymouth.	Senior House Surgeon, Victoria Hospital, Worksop.
	CORNWALL	
SPENCER, R. W., M.B., CH.B., M.R.C.P.	Consultant Pathologist to the West Cornwall Clinical Area.	Senior Registrar, Lecturer in the Department of Chemical Pathology, University of Leeds.

MOUNTAINS*

BY

DR. F. W. TERRELL HUGHES

I am a general practitioner in a rural practice. Perhaps the peace and quiet of the country tend to make one think more slowly and one is less likely to impute ulterior motives. When I was asked to become a member of the Med-Chi Committee, I thought no farther than that they perhaps wanted an elderly practitioner to represent that part of Somerset that lies on the southern boundary of Bristol. When I was later asked if I was willing to be elected President of this honourable and learned Society, my rustic mind received a shock. My first impulse was to refuse. I then remembered I was a G.P. and if I accepted I was being, so I thought, a representative of my G.P. colleagues and to refuse would, in a way, be letting them down. That is why I am here tonight, very conscious of this high honour bestowed on me by my colleagues in all the branches of medicine. Tonight I have roused myself from my rural relaxation, combed the straws from my hair and with the help of my friend at the epidiascope, hope to keep you interested in this talk about mountains.

As I began to plan this talk about mountains, I found there was much that could be related to medicine. Perhaps in general practice more than in any other branch of medicine, one is brought closer to the personality and environment of the patient and a consideration of these two things can be of help in his treatment.

Among mountains personality and environment matter a great deal and I have been often conscious of the personality of a mountain. To put it very simply, I have climbed one mountain that I have felt was always friendly, even though its moods might vary, and I have climbed another that has had to be tackled with greater care because it was unfriendly.

WHY CLIMB ?

No mountaineer when asked has been able satisfactorily to answer the question, Why do you climb? No one can explain to someone who has not felt it what a belief really feels like, nor if you have felt a belief is there any need to have it explained to you. Practice can often be defined in concrete terms, but motives can rarely be defined.

In the course of my experience in thinking, reading, and climbing, I have found two definitions of mountaineering. (1) Mountaineering is an unconscious search for beauty. (2) Mountaineering is the art of going safely in dangerous places. I had intended to discuss these two definitions separately, but as I wrote I found that one became involved with the other, interwoven and inseparable, and if I have given proper expression to my thoughts you will see how both of these definitions apply to true mountaineering. The second definition—"the art of going safely in dangerous places" could be applied to other activities as no doubt my surgical colleagues would agree, though theirs is a field in which I personally could not roam in safety. To go back to my first definition, the search for beauty, I do not mean we say "I must go and look for beauty on a mountain". It is rather that at some moment through some conscious act, one unexpectedly experiences a feeling of peace and relaxation, of achievement and even elation. This is experienced in art, music, philosophy and in religion, and Beauty is its name.

Painters cannot explain the need to paint and I believe an attempt to explain would end in a failure to paint. Given time and sufficient discernment laws could be

*Presidential Address to the Bristol Medico-Chirurgical Society, Wednesday, 14th October, 1959.

found to explain why a mountain always looks right and a painting or a photograph of a mountain sometimes looks wrong. The early masters rarely painted mountains. It is known that people looked upon mountains as places of dread and horror and painters and poets generally reflect the ideas and impressions of their time; they may be a little ahead of their time but they are influenced by mass suggestion. Wordsworth was one of the early romantics; he is not often read or quoted today but he was one of the first poets to see beauty in all nature and he was reflecting the thoughts of the people of his generation. They were beginning to see beauty and not fear in the higher and more remote parts of the earth.

There is also the inherited fear of mountains which was handed down and persisted through the Middle Ages. It is interesting to realize how this has become a thing of the past. It still persisted towards the end of the eighteenth century and was almost entirely dispelled by the inquiring mind of a scientist, in the broad sense of the word. He made science his excuse for climbing. In 1786 Dr. Paccard climbed Mont Blanc, justifying his efforts by the necessity to enquire into and make unprejudiced observations on conditions at this altitude. Others followed his example, nominally in the cause of science, and they were largely instrumental in ridding mountains of their myths and monsters. Yet there are still records of climbers who have felt the presence of another person in their team. Frank Smythe on one occasion divided his food ration into two parts and turned to hand one portion to the presence he felt beside him but found was not there. I think it likely that fatigue, lack of oxygen, and the tension of the situation explain this, but I can assure you the hallucination is very real.

Those who follow the ways of the hills are still often objects of astonishment. You may be asked if it is a question of heredity and when you say, "No, my father and my grandfather did not climb", the questioner turns away and sadly shakes his head, but you still go and climb hills. As you get away into the hills, you get away from mass suggestion and as you become aware of this freedom, relaxation becomes possible, and so your thoughts can take shape, influenced only by nature and its high hills.

As you climb you have to make decisions which involve an estimation of the strength of the mountains, you learn your limitations and know the mountain is always the stronger. You learn to make an effort to attain and you can share this exhilaration with those who climb with you. Much is said of the value of team games but, though mountaineering is not a game, I know of no team spirit that can compare with that of climbers, tied to a rope on a rock face. Whenever I was leading a climb with my brother second on the rope, he always knew if my hesitation before making a move was to decide how it could be best done or because I was anxious that I could not make it at all.

Fear must be respected on a mountain. I remember in my early climbing days being repeatedly told, if you become frightened, turn back. I do not think I have indulged in what may be called dangerous sports, and I believe than an analysis of the motives of those who have done so would show that they are not undertaken because they are dangerous. It is the challenge to achieve and overcome difficulties. I am absolutely certain that the real mountaineer does not climb for the fun of doing something dangerous. Thinking back to my early days of climbing and those men who taught me what I know of climbing, the first, second, and third lesson was always the technique and principle of climbing safely. It is the principle of always endeavouring to climb with a margin of safety, sometimes a very small margin, that produces the confidence that makes achievement possible even in great difficulties. One might say that perfect confidence casteth out fear. May I give you an incident in which, thinking back as I have many times, I am sure I had no fear and every confidence. Six of us were climbing in Switzerland. On my rope was a guide leading, then a girl, and myself third. On the other rope were three expert and experienced climbers. We were

going up a steep snow slope and our rope was some way ahead of the other when we came to a crevasse. This crevasse was about fifteen feet across, and it was spanned by a snow bridge; that is, frozen snow had left a possible means of crossing and the bridge was about three feet wide. I pushed my ice axe well into the snow and played out the rope as the guide went over on all fours, to distribute his weight. I saw the bridge shake and tremble a little during his passage. He cut steps up the steep slope on the far side and put his ice axe well into the snow and called to the girl to follow. She was safeguarded both by my belay and the guide's. Again I watched an even greater shaking of the snow bridge, but she made the crossing safely and, on the far slope, made herself secure with a belay around her ice axe. The guide called to me to come on. I told him the snow bridge would not take my weight, and for a few minutes we shouted to each other, he in his broken English and I in my broken French and then I gave in, and going on all fours began my passage along the bridge, my axe slung by its loop to my wrist. As I expected, when just over half way across, the bridge gave way. Being prepared for this I did my best to fling myself on to the far side, and the pull of the guide's rope enabled me to land with my arms on the slope and my legs dangling in the crevasse. It was a wonderful experience, first to hear the débris falling and never to hear it reach the bottom, and then to look down into the green depths of the crevasse. I then took the point of my ice axe, and digging it into the soft snow on the edge endeavoured to get a grip to pull myself out. Every time the steel point came through the soft snow and I could get no grip. I felt perfectly safe and had no feeling of alarm or fear at all. The two above me could not move from their belays as they were holding me, and I wondered what was the next thing to do. The smooth hard ice of the crevasse gave no grip for my nailed boots. I rested a moment and then heard a voice behind me say "Turn your ice axe round". I looked over my shoulder and saw the three experts on the other rope standing watching and grinning at my futile efforts. I turned my ice axe round, drove the blade instead of the point into the snow, obtained a hold and was soon out of the crevasse. It was a lesson learnt in technique, but at no time did I have any feeling of fear for the outcome.

If fear is deliberately and continually incurred, as it can be, it destroys those feelings that mountaineers value so highly.

FALLS

As regards a fall, it seems to be true that after the initial shock of losing balance or coming off a hold, fear is generally absent during the act of falling. There is a feeling of detachment. There are fanatics who say there is actual pleasure experienced during the act of falling. I do not know, for it is one of the pleasures I have never been in a position to enjoy; but I can give you the account of the distinguished and experienced mountaineer, Frank Smythe, who has recorded his thoughts after a fall*. He was climbing in the High Alps and he says it was due to his carelessness that the fall took place.

"When I heard Roberts's shout and the crash of falling rocks, my body instinctively braced itself to receive a shock. The shock came; I was unable to resist it, and found myself on my back sliding and bumping helplessly down the slabs of the ridge. Now, one half of my brain must have known subconsciously that twenty feet of slack rope separated me from the belay, but if it did know this, it was singularly reticent on the subject, and it was the other half that took charge, and this told me that I had been secured close to the belay, that the rope had come off and that I was certain to be killed. In view of my subsequent sensations, the certainty which existed in my mind that nothing could stop my falling and that I was to be killed, is interesting and

*From Frank Smythe's *The Spirit of the Hills*. Reproduced by kind permission of the author's widow, The Viscountess Molden, and of the publishers Messrs. Hodder and Stoughton, Ltd.

important. Nevertheless, even though I had assumed thus early that I was as good as dead, I made desperate attempts to stop myself, as I have already described. During the time that I was doing this, a curious rigidity or tension gripped my whole mental and physical being. So great was this tension that it swamped all pain and fear, and rendered me insensible to bumps and blows. It was an overwhelming sensation, and quite outside my experience. It was as though all life's forces were in process of undergoing some fundamental evolutionary change, the change called death, which is normally beyond imagination and outside the range of ordinary human force or power. I felt that power which alone can separate spirit from body—death. I know now that death is not to be feared, it is a supreme experience, the climax, not the anti-climax of life." (We who see people near death should find his opinion significant.)

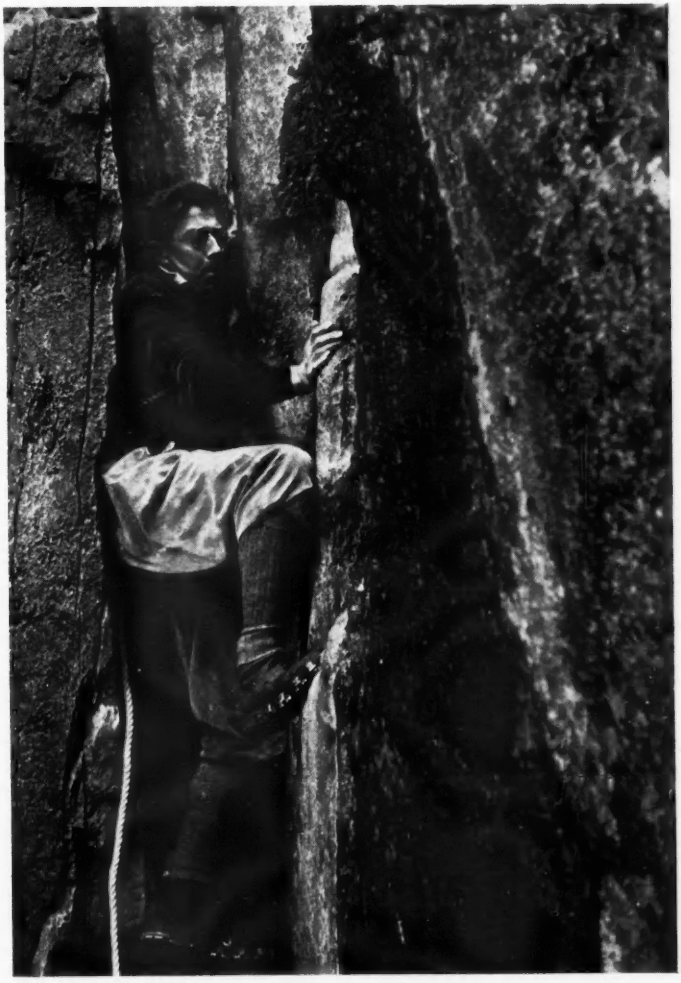
"For how long I experienced this crescendo of power I cannot say. Time no longer existed as time; it was replaced by a sequence of events from which time as a quantity or quality in terms of human consciousness no longer existed. Then, suddenly, this feeling was superseded by a feeling of complete indifference and detachment, indifference to what happened to my body, detachment from what was happening or likely to happen to that body. I seemed to stand aside from my body. I was not falling, for the reason that I was not in a dimension where it was possible to fall. I, that is my consciousness, was apart from my body, and not in the least concerned with what was befalling it. My body was in the process of being injured, crushed and pulped, and my consciousness was not associated with these physical injuries, and was completely uninterested in them. Had the tenant already departed in anticipation of the wreck that was to follow? Had the assumption of death—when my slide was not checked by the rope I assumed death as certain—resulted in a partial dissolution of the spiritual and physical? Was it merely a mental effect due to a sudden and intense nervous strain? It is not within my province to discuss that which only death can prove; yet to me this experience was a convincing one; it convinced me that consciousness survives beyond the grave.

"Had I died and passed on to another plane, I might have carried one memory with me. As I shot down the slabs and out over the edge of the sheer precipice, I saw stretched before me and below me the far-reaching, level, sunlit ocean of cloud, out of which we had climbed; I seemed to be diving straight into it. Above these clouds the sky was unclouded, a deep, profound blue from which the sun shone with dazzling radiance. I should have taken with me a memory that a king might have envied.

"Then I found myself hanging on the rope. The fact that I can remember no shock, and that I was not stunned, for my head received no blow, is interesting, as it bears out what I have already written on the feeling of detachment that was a feature of the fall. It was as though I was brutally dragged back to earth and earthly sensations. Simultaneously with the realization that I had not been killed, that something had arrested my fall, came fear. It was a curious, paradoxical thing to happen. During the fall I was not afraid, and now the fall had been stopped I was desperately afraid. I clutched and clawed at the rocks, and gained a footing and a hand-hold. I paused for a moment to try to still the thumping of my heart and the clamour of my lungs, which had been squeezed in by the pressure of the rope. Then I climbed, somehow or other, up to the ridge."

THE MOUNTAIN RESCUE ORGANIZATION

If you take the road from Capel Curig in North Wales, towards Snowdon and the Llanberis Pass, you come upon a delightful building which is the Pen-y-Gwyrd Hotel. From here, under the leadership of Christopher Briggs, goes out the Mountain Rescue Organization, when it is called upon to help those who have been unfortunate enough to have had an accident on the mountain.



"'*Climbing*' *in a rock chimney.*"

"On a rock face."

Many accidents are avoidable and learners cannot be too particular in observing and acquiring the technique their leaders are so willing to teach. One cannot afford to make mistakes when climbing, and avoidable accidents bring disrepute to one of the finest enterprises men and women have undertaken since the eighteenth century. A climb that is within the scope of a moderate climber in good weather may test the skill of the most experienced if the weather changes. When setting off climbers should always leave information of the mountain and climb to be attempted. The members of the Rescue Party are devoted and experienced climbers with an intimate knowledge of the mountains of Snowdonia and will always endeavour to bring an injured climber off the mountain to the road where the ambulance is waiting. They have special equipment but the rescue is often hazardous and may take many hours of exhausting work to achieve. It behoves all those who climb to respect these men and do their utmost to avoid imperilling the lives of those who are always ready and willing to give help when it is needed.

CHALLENGE

When we think of the Matterhorn in the days of Whymper, the first man to climb it, and Everest in our own day, it may well be said that these climbs were attempted and finally achieved because they were of outstanding peaks and their "conquest"—would create prestige. Whymper's first comment on the Matterhorn are quite derogatory, but the mountain finally captured his imagination and he came to feel its uniqueness and beauty.

Men had explored and climbed in the Himalayas for some years before Everest was attempted, but when you look at these pictures you must admit that to a mountaineer it is a challenge that is difficult to ignore. A great deal of mountaineering went into the successful climbing of Everest and Sir John Hunt and Sir Edmund Hilary were the first to admit they climbed Everest on the shoulders of their predecessors. A short account from one of the earlier climbers I think will be of interest as an example of the effort and hazards that were experienced.

Somervell, a London surgeon who addressed this Society on 16th May 1923, his subject being "The Problems of Living at High Altitudes", was in 1924 one of five men who stood at 28,000 feet on Everest. He and Norton were fighting their way up towards the 28,000 feet mark, and they had reached the stage where they had to take ten breaths for every step and sit down to rest every five minutes. Their reconnoitering done, they turned to go back to their last camp. Norton was in front and it was getting dark, and they were not roped. Somervell had one of his fits of coughing from which he had been suffering and dislodged something which stuck in his throat so that he could not breathe, either in or out. He could make no sign to Norton who had gone on, so he sat down on the snow to die. Finally he made one great effort, pressing his chest with both hands, and the obstruction came up; he coughed up a little blood and was able to breathe more freely than he had done for several days. The obstruction was a slough of mucous membrane lining the larynx, the result of frostbite due to the rapid inhalation of very cold air for so many hours a day.

Both on snow and rock effort and concentration are required. Picture I was taken on a rock climb in Wales, and it shows the leader in a rock chimney using the technique for this ascent and you can see the attitude showing concentration and effort. A different technique is employed for a crack as distinct from a chimney, but this also requires absolute concentration.

When on a rock face, to get the maximum pressure on the holds with hands and feet, the aim should be to avoid hugging the rock. In Picture II is a very good example of this position, the feet especially are pushed into the foot holds.

Sometimes in descending a cliff or snow slope the only route is to negotiate an overhang. This can be done by the use of ropes but the problem is to get the last man down. An abseil is the answer. The rope is doubled around some belay above the

overhang and then passed over the shoulder and under the thigh of the climber. When the climber has lowered himself to the rock beneath him the doubled rope can be pulled from the belay.

REWARDS

On a mountain I have found that both the opportunity and the desire to stay quiet not infrequently happens, and occasionally one reaps a tremendous and unexpected reward. I would like to give you an account of an experience the memory of which has remained fresh with me all my life. It is necessary to tell you briefly the incidents that led up to this great moment. When I was in India four of us decided to go into Kashmir, not by the orthodox route, but by the pass at the eastern end of the valley, provided it was open, it being the middle of May. We arrived at the foot of the pass and engaged nineteen porters to carry our kit, the loads having to be light as the way was steep. We set off before it was light, still uncertain whether Kashmiris had yet crossed and made a track. In a short while I became impatient of the slow pace and the presence of porters on the rough track and went on up alone and in due course the party behind me were out of sight. The track was steep and rough but not too hard going until at about 9,000 feet it divided right and left. I turned right but in a short time the track appeared to peter out on to a precipice of five or six thousand feet. I turned back and took the left hand track; this soon became the route for an ice stream, and so I thought the only thing to do was to go straight up. The climbing at first was over the rocks that were not too difficult, and then towards the 10,000 foot level I came on to snow, and visibility was reduced to about sixty feet by cloud. I went over the snow slope and in due course found a hut—this I knew was for Kashmiris crossing the pass who might be caught in a blizzard. Not knowing in which direction the track over the pass was, if it existed at all, I made tracks from the hut north, south, east and west, finding my way back to the hut on my own tracks, but failing to find the Kashmiri track down into the valley. I decided I must be bolder, and reasoning that the track would be east of the hut made a much longer journey and came on to a narrow track in the snow going north and south. This must be the Kashmiri track. I followed downhill towards what I hoped was the Valley of Kashmir but the cloud still gave me very little visibility. After descending about 1,000 feet I saw a pinnacle of rock with a flat top and decided to rest a while. It was about 3.0 p.m. and I had been going since early morning without rest and without food. As I sat on my pinnacle I noticed the clouds were rising. I watched almost breathless with anticipation as they lifted like a curtain in an enormous theatre. Presently I saw below me my first view of the Vale of Kashmir. The river Jhelum wound its way like a silver snake along the valley and on each side were the flooded rice fields and the brilliant yellow of the saffron in full bloom. They looked like squares of gold and silver in the bright sunlight. The clouds continued to rise and soon before me across the valley were revealed the peaks of the main Himalayan range and among them that queen of mountains Nanga Parbat, the fifth highest mountain in the world. I have no idea how long I sat and drank in the scene and experienced utter peace. I must admit that later, distant calls and the arrival of the party with food was not unwelcome, but their reproaches fell on deaf ears and have been forgotten. That one memory filled my day and has remained with me ever since.

You, too, must have had your great moments; keep them and cherish them, they may stand you in good stead one day.

"Only a hill, earth set a little higher
Above the face of earth: a larger view,
Of little fields and roads: a little nigher
To clouds and silence: what is that to you?
Only a hill; but all of life to me,
Up there, between the sunset and the sea."

When you have been in general practice, especially in the country, for a long time, you establish a relationship with your patients which is unique. You may also establish close and enduring friendships among your patients. These friends will come to you with their troubles, which may not always be medical ones, but as their friend and physician you will help them with your advice and guidance. But this friendship cannot be entirely reciprocal. If you yourself should be in trouble, and perhaps pass through the dark night of sorrow, you may want to look for a friend for help and guidance, and you may find that there is no one to whom you can go. Your friends have always looked to you as their friend and physician, as a rock which is secure, on which they can rely; you therefore feel that if you go to them you make yourself vulnerable, that they will not look upon you as someone set apart who is absolutely secure, and you feel they may never have again that complete confidence in your help and guidance, because you have shown that you too have weaknesses. So you turn away and you feel, very, very lonely. Many of you will have found a solution to this, some in music, some perhaps in painting or even in drama. I count myself fortunate in being among those who have found consolation by having been alone on a mountain. "For there is much comfort on high hills and a great easing of the heart."

MANAGEMENT OF SEPSIS

BY

HERBERT K. BOURNS, F.R.C.S.

Surgeon-in-charge of the Casualty Department, Bristol Royal Infirmary

Infection requires a host, an organism, and some other factor. This conditioning factor is unrecognised in many cases, but if sought in each case it often comes to light. It is important to look for it, because if we know what has started the process of sepsis, we may be able to remove it.

THE ORGANISM

Many patients are carriers of a virulent organism, particularly the staphylococcus. The common site for this is in the nose. Thus in a recent investigation in Bristol it was found that of people who had not been in contact with a hospital for at least a year, over 40 per cent were nasal carriers of staphylococci[1]. Other common sites for harbouring pathogenic organisms are the perineum and throat. Most nasal carriers are also skin carriers, so it is easy to see how these patients can be infected by their own organisms. Recurrent boils or abscess formation should always lead one to swab these areas. The removal of the reservoir of the germs will usually stop further abscess formation.

In Birmingham in 1956, 95 per cent of septic fingers were due to staphylococci[2]. In the Bristol Royal Infirmary in 1957, 90 per cent were due to this organism and 10 per cent due to streptococci[1]. (These figures refer to infected fingers from which pus was available for culture.) The results in Bristol further supported a clinical impression that the *phage* type of the staphylococcus was related to the severity of the infection. Thus the troublesome Phage Type 80 *Staphylococcus* which was first isolated in 1953 by Rountree and Freeman (1955) in Australia[3] has enhanced virulence, and so infection with it leads to sloughs and tissue damage with considerable toxaemia.

> A little boy was admitted with a partial-thickness burn of about twenty per cent. His initial course was satisfactory. There was a sudden deterioration in his condition and he became unconscious. Meningeal infection was suspected but lumbar puncture did not confirm this. The burnt surface was infected and the cause of the severe general reaction was shown when Type 80 Staphylococci were grown on culture. He rapidly improved when erythromycin was given in large doses.

The "phage types" which are resistant to more than one antibiotic are usually more virulent. Thus the spread of resistant organisms may lead to increase in the incidence of more serious infections.

LOW RESISTANCE

Intercurrent diseases may lower the resistance either of a patient as a whole, or of his tissues locally. General conditions, such as diabetes mellitus, have to be looked for in all cases with infection and particularly in patients who appear to be healthy.

Healthy patients are more susceptible after an operation. "The increased congregation of more susceptible hosts" is probably one of the reasons for the increase in staphylococcal infections in hospital[4]. Since patients nowadays are discharged from hospital so early in their recovery period, this susceptible state persists into home life, and in this way some patients develop infections from their own home organisms which normally would not affect them.

LOCAL FACTORS

Local trauma, with haematoma formation and divitalized tissue even if only present for a short time, may lead to the formation of an abscess. The conservative treatment of haematomata always carries the risk of infection, because organisms gain access to this extravasated blood. Moreover, fat necrosis as the result of contusion is much more common than is generally recognized; it gives rise either to immediate fluctuation and abscess formation, or to organization, fibrosis, and the appearance of an unexplained "tumour". This "tumour" is a firm and painless lump which may appear many months after the original trauma.

Neuropathy and vascular diseases have also to be considered.

Recently a patient had a "septic finger" for two years, despite all efforts to produce healing, because she had a lesion of the spinal cord affecting her sensation.

Peripheral vascular disease of all types should be considered, especially when there is infection of the hands or feet. If the circulation is inadequate chronicity of the infection is usual; but the real danger is the onset of gangrene of the tips of either fingers or toes. Whole toes or parts of fingers may have to be amputated in order to limit the infection to a region where the body defences are more adequate.

BONE DISEASE

Bone disease is a potent source of trouble in infection. A sequestrum may form when the blood supply to the bone is inadequate, and as a result the process will not heal until the dead bone has separated and has been extruded. This is a troublesome feature in pulp space infections of the fingers; but it is less common now that incisions are correctly placed.

BREAST ABSCESS

In breasts, the site of an abscess is very often a lobule with retained milk. Either weaning or inefficient feeding may be the cause, and either lack of hygiene or cracked nipple, or both, the precipitating factor. The complete emptying of all segments of the breast, at least once a day, will reduce the incidence of breast abscesses. More vigorous measures may help to resolve an abscess that has begun to form.

A mother was sent to hospital with a large indurated area in the lower half of the left breast. She had had five daily injections of a mega-unit of crystalline penicillin. She was weaning her baby and had been advised to use firm support for her breasts and only to empty them once a day. The treatment advised by the hospital was to stop all antibiotics, cease compression and to empty her breast three or four times a day. Within two weeks, the "abscess" had disappeared and the breasts became dry at about the same time. Much of this lump may well have been due to a galactocele and the use of a breast pump enabled the congestion to be removed, so that the affected area drained properly. The patient was saved pain and discomfort by this simple treatment.

MIXED INFECTIONS

Chronic infections may become secondarily infected. This secondary infection will not clear up until the primary one is dealt with. Two recent cases illustrate this point:

A young boy had a large patch of infection on his forehead for many months. In hospital ringworm was demonstrated and when this had been treated the pus quickly cleared up.

Tuberculous lymphadenitis is often a cause of persistent sepsis, even when a pyogenic organisms has been identified.

Thus, a little girl had an abscess in her left groin; this was incised and she was discharged to the care of her own doctor. After some months, however, she was sent back with a granulating wound and profuse purulent discharge, for opinion as to what further antibiotic might be used. Excision of the wound and a diseased gland at the base of the wound revealed the cause of the trouble, for tubercle bacilli were demonstrated. The condition quickly cleared with excision of the affected gland, together with appropriate chemotherapy.

EFFECT OF DRESSINGS

The type of dressing used may cause an infection either to persist or to spread. Gauze impregnated with soft paraffin is greasy, and does not facilitate the escape of wound exudate, nor does it allow the skin around the wound to be cleansed without the use of a fat solvent. The ulcer and the surrounding skin become macerated and so healing is delayed. Watson[2] found that changing from dry dressing to vaseline gauze delayed healing time by an average of two days in septic fingers. "Carbonet" has superseded both dry dressing and vaseline gauze and I have found it to be one of the best of the nonadherent sterile dressings[5]. It is water-soluble and so allows the wound to "breathe".

Cod liver oil impregnation of a wound leads to delay in healing because the tissues take up the large droplets and cannot dispose of them. The absorption leads to foreign body reaction. The wound edges become changed from healing granulation tissue to oil granulomata; this leads to poor healing and surrounding fibrosis.

> A patient who was sent to the Bristol Royal Infirmary had sustained a deep wound above the right knee four months previously. The wound was unhealthy, the edges were fibrotic, and there was a persistent sero-purulent discharge. The wound was excised and the tissue removed was sent for histological examination. Many oil droplets were seen. The patient volunteered the information that for the first month after her injury the wound was packed with dressings impregnated with cod liver oil. The wound was sutured after excision, but it was another four months before it healed soundly. Our excision had not been wide enough, but this could not be helped, because the wound was so close to the knee joint.

"ANTIBIOMA"

Antibiotic granulomas or "antibiomas" have been reported from time to time[6,7]. In such cases, the acute inflamation subsides but an indurated area remains for a long time. This is caused by the doctor's failure to diagnose the presence of pus, and his consequent failure to drain it; all abscesses should be opened and drained, even when the local and general reaction to antibiotic therapy appears to have been very satisfactory. Pus must always be drained, for if an abscess is not opened it may become inspissated and then slowly organises. This does not happen in all cases; the usual course of events when antibiotics are given without incision is for the abscess to persist as a fluctuant area; in time, the signs of acute inflammation return, unless the abscess bursts and discharges itself. This re-activiation may be caused by a fresh organism, or by the original one which multiplies afresh once the antibiotic is withdrawn. Antibiotics, of course, have a place in the treatment of sepsis, but they must not be employed as a substitute for drainage. They are of great value in combating systemic spread, but early incision must still be the order of the day if chronicity is to be avoided.

TREATMENT

Treatment may be considered under two headings; treatment of the Patient and treatment of the Part.

Treatment of the Patient

To help a patient to combat any but the most trivial of infections, rest is essential. Many patients will not readily agree to rest when it is first suggested to them, but not infrequently they have to concede the necessity for this before the treatment has gone very far.

Pain should be relieved. But patients will frequently wait for medical advice before they will take such simple remedies as Aspirin or Tabs. Codeine Co., both of which are usually adequate in the average infection.

One should remind the patients to take more fluid by mouth. Many patients lose their appetite and so they do not have their normal meals. Since they do not wish to eat, they often omit to drink.

The patient must be given an explanation of his treatment and a guarded prognosis as soon as possible.

Treatment of the Part

Like that of the patient as a whole, this must commence with rest; a simple measure that is often overlooked. A sling is a necessity in most hand infections; rest in bed or in a chair with the foot elevated may be necessary for the lower limb.

Relief of pain is served by providing adequate dressings to support and protect the inflamed area. The frequent application of heat is comforting, whether by hot fomentation or heat lamp. Poulticing, on the other hand, has a number of serious drawbacks; the poultice tends to stick, it obscures the lesion from clinical inspection, and it causes scalding and maceration of the skin and superficial tissues. Patients, in order to prolong the effect, usually apply poultices far too hot. Unless changed frequently, poultices become "cold compresses".

If we wish to "draw" an abscess, glycerine and magnesium sulphate paste is one of the better local applications. Daily dressing is essential but there is little to be gained by increasing the frequency to more than twice in the twenty-four hours.

Incision

Relief of pain is achieved by relief of tension in the infected part. When swelling persists and becomes localized, suppuration is usually present. Incisions must be carried out as soon as fluctuation is present or when deep pus is suspected. It should be remembered that an abscess cavity is not a linear structure, so that, on incision, the cavity must be explored either with a gloved finger or by sinus forceps. Once its limits have been defined, it must be "de-roofed", so that pus will not "pocket"; in this way the wound will not close until the abscess cavity has filled in. Therefore, incision is not just a stab under inadequate anaesthesia, but a planned operation in an anaesthetized patient, without any hurry, so that the surgeon can carry out a thorough inspection of the abscess cavity. Only in this way will adequate drainage be achieved and speedy healing attained.

I do not advocate "incision and suture" of an abscess. This form of treatment has been recommended mainly by Ellis of Leeds[8]. After incision the cavity is curretted and then when all pus and debris has been removed, the wound is stitched. Pressure is applied to prevent haematoma formation and antibiotics are given. This is stated to produce early healing and less scarring. This is a practice which has few advantages and many disadvantages. Firstly, I am sure that to be successful this treatment must be carried out only by an expert; in other words it cannot be applied generally. Secondly, it is based on the principle that the organism (which can only be obtained at the time of the incision) will be sensitive to whatever antibiotic is being used. However, we do not *know* the organism or its sensitivity until forty-eight hours have elapsed. Thirdly, the currettage of the abscess cavity leads to disruption of the barrier already laid down round the abscess cavity, and to damage of defensive cells growing round the abscess. Fourthly, a stitched abscess does not heal any more quickly than an open abscess that is thoroughly drained, and so there is little difference in scarring.

If the infecting organism is sensitive to penicillin this antibiotic should be given. It is best given by intramuscular injection, and in the average case adequate dosage for a few days is better than low dosage for a long time. However, prolonged use of antibiotics is essential in bone, tendon, and joint infection. These tissues are all "specialized" and must be preserved at all costs if normal function is to be restored. Antibiotics may also be necessary in patients who are ill from other causes, such as diabetes, tuberculosis, nutritional disorders; or when they have had drugs such as corticoids. In recurring infections and in reparative processes, antibiotics may have to be given for a long period.

In a carbuncle, skin loss may be considerable. When the slough has been removed and a healthy granulating surface has been produced, the use of a skin graft should not be rejected for fear of infection. Identification of the type and sensitivity of the causative organism should be obtained, and then the defect should be covered with skin, while the appropriate antibiotic is given to cover the procedure.

Restoration of function

Healing by fibrosis as the result of granulation tissue will lead to loss of function and stiffness. Early restoration of movement is desirable. Movement, however, must not be encouraged until the infection is under control. One must persist with rest until the inflammatory process has settled completely. As soon as the infection has been localized and drained, the part will move easily. If movement is allowed too early, further spread of the infection will be promoted and chronicity will be produced. Apart from this, the patient's confidence may be undermined because early function will be painful.

> In a recent case, a doctor had a boil on the right wrist. It was not very painful so he played a round of golf. Within twelve hours the surrounding oedema was testimony to the increase in his pain; there was lymphangitis of the arm and lymphadenitis of the axillary glands together with a raised temperature demonstrating the general toxaemia. Twenty-four hours rest, without antibiotics, caused a return to the previous localized state.

In infections of the hand immobilisation in the position of physiological rest does not have any permanent unpleasant results if early healing is attained. Even tendon sheath infections and exposure of the tendons themselves may be overcome if the wound is closed early. Scar tissue dissolves in time, so that one must not be discouraged by early lack of mobility. The final result will be much better if rest is maintained until healing is complete.

Dressings

The dressing must be sterile. As mentioned above, it should be non-greasy and non-irritant. "Carbonet" is one of the best at present, because it is easily sterilized and harmless to the tissues. Dressings should only be changed when the volume of discharge makes this necessary. Dressings are intended as a protection for the wound; they should therefore be large enough for this purpose. Constriction should always be avoided; this particularly applies to the use of "Tubegauz" with which the unskilled may easily produce a constriction at the edge of the dressing by excessive twisting or pulling during the application of the bandage. (The manufacturers of this bandage are well aware of this danger and warn against it in all their literature.)

Dressings must be kept out of water. If by accident they become wet, then they should be changed. On the other hand, enclosure in a water-tight cover is bad because, in the first place, many covers are so inefficient that moisture will inevitably get in, and secondly the cover prevents the natural heat of the part from promoting the drying of the moist dressings. Incidentally, many do not realize that a watery dressing only remains wet for about half an hour unless covered by a water-proof cover. Yet if dressings are covered in this way, maceration is soon produced so that healing is delayed.

In conclusion, management of septic lesions should consist of rest for the patient and the part, antibiotics, adequate incision and drainage, search for any possible cause, promotion of early healing, and finally mobilisation.

REFERENCES

1 James, W. and Adler, V. G. To be published.
2 Williams, J. A., Meynell, M. J. and Watson, A. B. (1956). *Brit. med. J. i*, 716.
3 Rountree, P. M. and Freeman, B. M. (1955). *Med. J. Austr.* **2**, 157.
4 McDermott, W. (1956). *Brit. med. J. ii*, 837.
5 Bourns, H. K. (1958). *Lancet ii*, 420.
6 Stammers, F. A. R. (1953). *Brit. med. J. i*, 272.
7 Mills, C. P. (1953). *Brit. med. J. i*, 1427.
8 Ellis, M. (1951). *Lancet i*, 1038.

X-RAYS IN EVERYDAY LIFE

LONG FOX MEMORIAL LECTURE—13th OCTOBER 1959

BY

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Many of those who have had the honour of delivering this lecture were, or still are, distinguished men. I am privileged to find myself named among them, but this has made me acutely conscious of my own shortcomings. This is no mock modesty, for what can a radiologist discuss apart from technical aspects of his work, that is not well known to experts in other fields? For X-rays are the handmaiden of experts in all scientific walks of life and lie within the experience of the man in the street.

There is however, one course open to me: to take a cross-section of life and to see how and where X-rays enter into the lives of us all. I think I may surprise some of you, I hope I may interest all.

X-rays are a form of energy. They are a form of electro-magnetic radiation, and part of the whole spectrum of electro-magnetic radiation, of which visible light is another part. At one extreme are wireless waves, towards the other extreme X-rays, wavelength being the fundamental difference between these various forms of radiation. Whereas wireless waves have a wavelength measured in metres, those of X-rays are measured in Ångstroms (which are units of length about the size of atoms).

X-rays have several properties: They can penetrate matter; they have biological effects; they have a photographic effect, and can be diffracted. We have made use of all these properties; one—the biological effect—has inherent dangers, and I shall discuss these at some length later.

In the modern community life which has evolved in the Western part of this planet, some of the scientific aspects of which are now being applied by other communities, X-rays have come to play an integral part. They are part of the whole, part of our culture. Advances in civilized life are achieved in stages: research is undertaken; some fruits of this are applicable to everyday life; those that are useful are developed and then may influence our way of life. Often it is only the end that is apparent, the means to the end is not evident, so it is that the means to the end becomes accepted and incorporated in our life without the community at large realizing this.

APPLICATION OF X-RAYS IN MEDICINE

Use of the Biological Effects. In the field of medicine use has been made of the biological effect for the treatment of patients. The effect of X-rays on living tissues is to cause an increased blood-flow to those tissues and then with higher doses to cause the death of the tissues. At one time it was hoped that this might be a universal cure for cancer and extravagant claims were made for it. These claims were not all substantiated and as a result the method fell for a time into disfavour. Fortunately there has been a resurgence and it is a fact that many people to-day owe their lives to it, for in selected cases and certain types of cancer it is the treatment of choice with remarkable results, apparent complete cure being procured. In many other cases the final outcome is hopeless but palliation can be obtained and months and even years of comfort and useful life achieved.

This form of treatment is also an accepted regime for certain types of arthritis and rheumatism. In skilled hands remarkably good results can be obtained in many

instances. It is not a cure, but it can relieve pain, and may sometimes halt progression of the disease.

Again for certain types of skin disease this is the treatment of choice, cure often being obtained regularly by this method where other methods fail.

A newer application of the biological effects of X-rays is to sterilize medical equipment and vaccines, and to disinfect packaged products and foods. Bacterial and virus contamination can be eliminated by irradiation. The method is already being used, and at the present time a new plant is being built at the Wantage Radiation Laboratories under the direction of the Atomic Energy Research Establishment, for testing the process on a large scale—it is hoped there to render sterile three tons of equipment a day.

X-rays in Diagnosis. Next, in the field of medicine, the property of X-rays to penetrate matter and produce a photographic effect has been put to use. This is the application with which most people are familiar—the field of medical diagnosis—my own specialty. It is now a vast, complicated and expensive science. It can be classified mainly into four categories, prophylactic, diagnostic, control of treatment, and research.

The Prophylactic use includes the detection and prevention of spread of disease. It was early employed for occupational diseases such as coalminer's pneumoconiosis and silicosis. More recently—in the post-war period—pulmonary tuberculosis has been virtually eliminated. This has been due to the triad—early radiological diagnosis, new effective anti-tuberculous drugs and an increase in the general standard of nutrition and housing of the nation.

In practical medicine, firm and definite diagnosis is an essential pre-requisite to proper treatment. Under many conditions, radiology has its part to play in diagnosis. During the years of development of this science, there have been periods of abuse, when it has been regarded as the be-all and end-all of diagnosis. We have fortunately come through that phase and radiology is now taking its place in proper perspective—as a useful diagnostic aid in the diagnosis of many ailments, alongside other tools which aid the art of the doctor—clinical acumen, experience, laboratory methods and so forth. In its proper place and used logically, it is invaluable; but what experienced doctors realize, though this is unfortunately not yet realized widely by the laity, is that X-rays have their limitations and pitfalls.

In the control of treatment the great benefits of radiodiagnosis are well illustrated in that common misfortune—fracture of the femur in the elderly. Without X-rays a patient might have to spend many months in bed; but with proper radiological facilities it is now common practice to nail the hip so that within a few weeks the patient can be back home and doing her shopping. In medical research the use of radiological methods seems endless. Usually the X-ray method is not the whole, but is merely part of a team approach to some problem. Thus, in the rapid strides that have been made in the surgery of the heart, radiological investigation has been an essential pre-operative measure to establish a diagnosis and so influence surgical approach and treatment.

VETERINARY USES

In veterinary work X-rays are being used increasingly both as a diagnostic tool and as a research method. As a diagnostic tool they can demonstrate anything from urinary stones to confirmation of pregnancy, from lung diseases to fractures. The animal examined may be anything from an elephant to a bat. At the London Zoo now there is a treatment centre with a well-equipped operating theatre, provided with full X-ray facilities (see Plate VIII).

As examples of research methods X-rays have been used to investigate the gastro-intestinal tract of ruminants and recently an entire book has been devoted to this subject. Similarly X-rays are now in use to investigate the cause of and treatment of rickets in South American monkeys. Some Scottish sheep do not thrive and do not produce

live young when grazed on certain lowland pastures. By studying the delay in ossification and the degree of mineralization of bones of these sheep, it has been possible to incriminate the mineral content of the soil on which the pasture was growing. In some cases it has been possible to rectify this, and to show improved mineralization of the sheep's bones.

TESTING WORKS OF ART

In non-destructive testing of antiquities and works of art, X-rays have a valuable place. For example, at the British Museum there is a laboratory for such testing and X-ray apparatus is amongst its tools. There the work done consists of the examination and identification of such objects as bronzes, iron, marble and ceramics and the examination of these for flaws, cracks, repairs, artefacts, inlays, and for determining the way they were made. There I have seen jet beads being examined to determine the direction of their holes, bronze figures to see if they are in one piece or whether the head has been joined subsequently; articles that cannot be opened (e.g. a mummy) examined to see what was inside (see Plate IX), pots to see if they have been broken and later repaired, bronze sword handles to see their method of attachment, and clay tablets for identification of inscriptions. What is demonstrated by this method may contribute to knowledge of structure, and often influences the decision to purchase or the price to be paid if flaws are demonstrated. In the realm of conservation most objects, before restoration or routine maintenance is undertaken, are examined by this method.

At the National Gallery, Dr. Rawlins, the Physicist-in-charge of the Research Laboratory has devized for non-destructive testing of paintings an X-ray method based on the differential X-ray absorption of the various thicknesses of the different pigments. Discrimination between old and modern paintings is possible because lead pigments were used in the older paintings, whereas more recent oil colours are less opaque to X-rays. In addition, modern priming is more opaque than ancient priming and accordingly the radiograph of a modern painting reveals no features of the visual image other than the highlights. X-rays thus reveal much of the artist's technique, the nature of the pigments he used, and details of his brush work. In this way old masters of the South European School, can be differentiated from those of the North European School. Both groups painted on wood panels, which was usually poplar, and they primed these with a covering of gypsum on which they drew in chalk, then painted. Rafael, an example of the Southern European School, would paint the surround heavily with lead paints, but only the highlights of his figure, leaving the flesh figure in gypsum. An X-ray of this shows an opaque surround and a non-opaque figure. Rubens, on the other hand, an example of the North European School, painted the figure heavily with lead paints, but the surround he painted less heavily with lakes and other less dense paints. An X-ray of this shows the reverse of the other. In this way also the alterations by the original artist, modifications by later painters and forgeries can be detected.

The method is also used routinely before restoration to show cracks, breaks, and blisters; once these have been demonstrated they can be readily repaired.

DETECTION OF CRIME

In forensic work and criminology this tool is again useful. For instance, all mail entering scheduled establishments, e.g. Harwell, is screened fluoroscopically. In Tanganyika, I have seen all workers leaving the Williamson diamond mines each day being screened fluoroscopically, to see whether or not they are carrying away diamonds. Localization of foreign bodies is of course a simple procedure, much the same technically whether it is localizing a bullet in a corpse, or say, a swallowed hair grip in a child, which is a daily event in my department. With the police in Bristol, we have been trying to devise a way of X-raying the fingerprints of those corpses from whom

the outer skin surface has been eroded; for when this occurs it is impossible to obtain finger prints by normal photographic methods. Similarly, it is possible to examine postage stamps by the use of very soft X-rays, even to see the watermark and to detect forgeries in this way.

X-RAYS IN INDUSTRY

First let us consider welding. Two metal surfaces are joined by a process, usually with the use of an oxy-acetylene arc, which melts the two adjacent surfaces and a third metallic source, and all three are allowed to intermix. Then on cooling this fuses together. If the technique of the craftsman is at fault, flaws may arise at the junction giving a joint which is insecure and may even be dangerous. Inspection of welds by radiography is now normal practice in many industries and in some it is compulsory.

In 1930 the United States Navy decided to accept fusion-welded steam vessels provided that radiographic technique became an accepted inspection procedure for these welds. In 1934, Lloyds Register of Shipping wrote this inspection technique into new codes for the acceptance of welded vessels. And now radiography is widely used for inspecting large welded structures. The type of defects that may be detected are blowholes, cracks (see Plate X), inclusions, large grain size, burnt metal, locked up stresses, porosity (see Plate XI), and so forth. Moreover, X-ray inspection is of great value in the training of welders and their attainment of approved standards. Insurance companies whose inspectors supervise every step of such procedures in many cases insist on their approval of both the X-ray department and the industrial radiologist.

This technique is now applied to all pressure containers (e.g. ships' boilers, gas-holders, steam generating plants, chemical reaction equipment, chemical containers such as those for butane or ammonia for refrigeraters, boilers for power stations, paint kettles for paint manufacturers); it is applied to oil pipe lines, ship-building, atomic power stations, railway engine construction, aircraft production, and in the constructional trade by the big contractors.

Next let us turn to casting. A casting is a piece of metal shaped in a mould which is a pattern of a shaped cavity prepared to receive molten metal. There are various methods of casting, such as, sand casting, die casting, centrifugal casting, precision casting, and shell moulding. They may be enormous as are some of the steel castings or they may be light alloy castings. Radiography is a routine method of inspection of these foundry products. It may reveal inhomogeneity in what is outwardly solid metal. This inhomogeneity may be due to contraction cavities (see Plate XII), gas evolved by the metal during contraction, inclusions, or interaction between the mould material and the liquid metal. Defects thus shown have influenced foundry technique considerably, thus shrinkage during cooling must be overcome by what is called "topping up"—the exact method of this topping up depends on the cooling curve of the metal concerned and the shape being produced.

X-ray inspection of castings for machine parts is widely used in the aircraft industry, and it is used extensively in the steel industry for inspection of tungsten steel, of die casts for printing presses, of accumulator grids and of machine tools. In any factory in this country where there is precision machinery, much of that machinery has been cast and much of it has been X-rayed during production.

In the aircraft industry, in addition to the welds and castings already mentioned, X-ray inspection of construction techniques and stress points is common practice. This is carried out both during construction and also after a specified number of flying hours (10,000) or a specified number of landings (500). What happens is this. During construction and testing, stress experts work out which spars and struts and components require examination. The radiology department then X-rays the parts concerned working out a technique for the examination of each part—not an easy problem when heavy X-ray apparatus has to be manipulated around an aircraft. For some examinations the apparatus has to be manhandled into the craft, whereas others

PLATE VIII

K-*ray of a Tiger's fore-foot showing osteomyelitis of the radius.* (*Taken at the London Zoo—courtesy of Mr. Graham Jones.*)

PLATE IX

A mummified bird removed from a tomb shown by X-ray examination without removing the outer casing. (Courtesy of Kodak Ltd.)

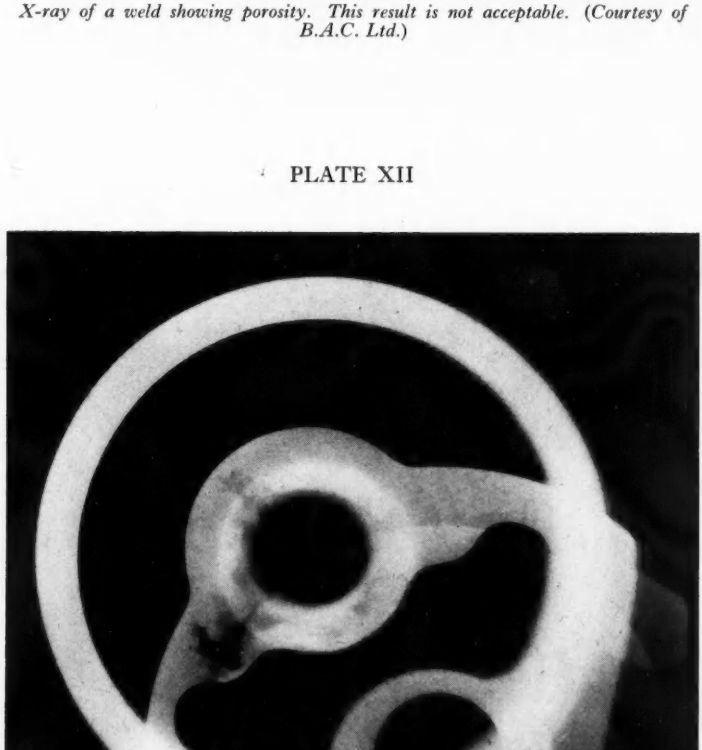
PLATE X

X-ray of the emergency exit of an aircraft where two metal surfaces have been welded together showing cracks and blowholes. These defects are not acceptable.
(Courtesy of B.A.C. Ltd.)

PLATE XI

X-ray of a weld showing porosity. This result is not acceptable. (Courtesy of B.A.C. Ltd.)

PLATE XII



X-ray of a metal casting showing contraction cavities. (Courtesy of Kodak Ltd.)

can be carried out from outside. Wings and body-work and undercarriages are examined at selected points. The technique for the examination of all these parts is then written into the instructions that go with the aircraft to the buyer. The faults that are detected in this way are cracks and fractures—metal fatigue. Some of these defects may call for the replacing of a spar, while some are merely splinted by rivetting metal plates across them.

There are other parts of aircraft which need inspecting radiographically when the plane is in commission. These include rivettings to see that the outer fabric is correctly rivetted to the spars, electric wires in propellers for the de-icing apparatus, and oil coolers after cleaning to see that all contaminants have been removed, for if all sludge and metallic foreign bodies are not removed engine failure may develop.

In industry, such as manufacture of rubber products radiological inspection of mouldings is widely used. For example, radiography is an essential tool in the manufacture of motor tyres. The rubber is moulded onto a fabric base. For research purposes fine wires are embedded in selected places in a tyre during manufacture, in order to follow any changes in structure during running. Individual cords in the fabric, and the continuity of them, are investigated by injecting liquid mercury which flows along the cords, and the tyre is then X-rayed. This technique is also used in the rubber industry to inspect golf balls, belting and hose.

Nowadays inspection of assembled objects by radiography is standard practice. Examples of this are wireless valves to determine correct positioning of grids, electric light bulbs, X-ray tubes (it seems rather paradoxical to X-ray an X-ray tube) and sealed hydraulic cylinders to isolate faults.

In the textile industry, cloths are inspected by radiography; and likewise it is possible to determine whether pearls are cultured or are natural.

Inspection by fluoroscopy is used on an even wider front. Fluoroscopy is the technique whereby X-rays are directed through the object being examined onto a fluorescent screen which an observer watches. The objects are usually put on a moving belt and move across in front of the screen giving the observer time to inspect for defects or foreign bodies and time to pick out any that he wishes to examine more fully. No permanent record, such as a photograph, is made in this case. This technique is used for inspecting packaged razor blades to determine whether any have been damaged by the packing machinery; for ascertaining the nature of glass used in the manufacture of clinical thermometers, to determine the accurate positioning of inserts in insulators, to detect the presence of foreign bodies such as glass in synthetic sponges, to eliminate faults and calcareous plaques from skins, particularly crocodile skins, before tanning, and to ensure centralization of the core and also bonding of joints in cable manufacture and so on. Fluoroscopic screening is also used in the food and confectionery industries. I have visited chocolate and sweet factories where anything from 2,000 to 5,000 boxes or packages are inspected a day, and where perhaps forty or fifty packages a day are rejected by the observer; these packages are opened and in fifteen or twenty, a metallic fragment is recovered, perhaps a chip from the machinery or a nail from a crate. Some bakeries use this method to detect opaque foreign bodies which may have been included with the dried fruit. Baby foods, sausages and pies, tinned or packaged foods and frozen vegetables are other everyday commodities examined by fluoroscopy. Many materials are screened in bulk before being tinned or used for manufacture, like peanuts, to eliminate stones. Some importers now inspect citrous fruits (oranges and grape-fruits) for crystallization, frost damage and puffiness in order to reject the bad fruit.

There seems to be no end to the ingenious ways in which X-rays may be used in industry. Viscosity of opaque fluids has recently been measured by X-raying a metal ball dropping through the fluid. The firm concerned was manufacturing ink for ball-point pens, and the viscosity and consistency of the ink are critical. This method of inspection solved their problem.

Flash radiography is another technique which is used to examine very rapidly moving objects by means of a single intense pulse of X-rays. Objects can be studied when they are beyond the reach of high speed photography with visual light, for example in explosions when the flight of projectiles is obscured by smoke and flame.

Micro-radiography is the taking of a radiograph with very soft X-rays through very thin sections. It can be used for biological specimens, paper, fabrics, or metals. Organic slices can be cut with a microtome; metallic slices can be cut at about one sixteenth of an inch thickness and then polished down further. The resultant radiograph can be magnified from 200- to 500-fold for study. This technique can be used to tackle such problems as the segregation of constituents in alloys, the distribution of elements in steel and the effect of any such segregation on machinability.

X-RAY DIFFRACTION

In 1912 von Laue discovered that the regular network of atoms in a crystalline substance provides a three-dimensional grating suitable for the diffraction of X-rays. The interaction of X-rays with the atomic pattern of a crystal depends on the similarity between the wavelength of the X-rays and the regular distances between the scattering centres in the atomic pattern. Inter-atomic distances are about one Ångstrom, so X-rays of about one Ångstrom wavelength will be diffracted at angles convenient for registration on a photographic film. From this, atomic arrangements can be calculated, and in this way our knowledge of atomic structure has been enormously expanded. X-rays have, by this method, disclosed the underlying atomic patterns not only of such recognizably crystalline substances as quartz and diamond, but also of metals and alloys, inorganic chemicals such as the various minerals in the earth's crust and of natural organic fibres such as silk and cotton and synthetic polymers like nylon and polythene.

From its earliest days it was apparent that X-ray diffraction was an analytical tool of great value which could be used to supplement physical and chemical methods. Now it has developed into a large science, with even the formation of an International Union of X-ray Crystallography.

The applications of this procedure which affect our everyday life are diverse. For example, impurities in petrol are analyzed thus by the petrol firms; the various crystal forms of silica can be differentiated for the manufacture of steel and glass; the crystal form of magnesium tungstate required for fluorescent lamps is critical and is identified by this method; in metallurgy the orientation of grains and crystallites in ingots have considerable bearing on the properties of that particular metal, as for instance the power of electro-deposited chromium to remain bright; the tensile strength of nylon may be increased very considerably by cold stretching which has the effect of producing a directionally orientated arrangement of molecules with respect to the fibre axis, all of which has been investigated and subsequently controlled by this method; similarly gloss and sheen may be affected by the molecular orientation, as shown by X-ray diffraction patterns.

ECONOMICS

The cost of all this is difficult to assess with any degree of accuracy. From figures made available by the Ministry of Health I have estimated that in the financial year 1957–8, the use of X-rays in the Health Service cost about £22,000,000. The cost in industry must be considerably less than that figure, but it is even more difficult to estimate. In the Health Service there are employed approximately 1,000 radiologists (or radiologists in training), 3,500 radiographers, 2,500 clerical and dark-room workers —a total of around 7,000. I have been unable to find a means of estimating accurately the number employed on this work in industry. The rate of work in some industrial establishments is greater than in medicine; for example in my department in the United Bristol Hospitals, a large busy teaching hospital, carrying out 70,000 X-ray

examinations a year, we process an average of 600 films a day. At the Rolls Royce Works in Derby which I have visited, the X-ray department, X-raying component parts of aero jet engines, processes 1,600 films a day and has an annual film bill of £48,000. There are about six or seven firms in the country (for example Stirling Metals and Kent Alloys) that each process over 2,000 films a day.

I understand from the film manufacturers that about 30 per cent of their production goes to industry and 70 per cent to medical uses, but this is not a strictly accurate yard-stick because of course many more of the smaller films are used in industry than in medicine, and cost is related to area of film used and not to the number of them. However, taking into consideration all these factors I estimate that there are about 2,000 workers on the industrial side of X-ray work, and that the cost to industry of the work is of the order of £7,000,000 per annum.

There is one other aspect to be considered here—the organization and number of people concerned with producing X-ray apparatus and films. Most of the firms manufacturing X-ray equipment are now subsidiaries of larger concerns and so again it is not possible to arrive at any exact figure of the number of people employed in the industry. The X-ray manufacturing side of these companies is not a thriving industry. Many thousands of pounds are poured into research and most firms just manage to remain solvent. If they had not the backing of their parent companies—for example, on the continent, Philips Ltd. of Eindhoven manufacture X-ray equipment but the vast safe umbrella of the financially successful electric lamp manufacturing company is there to shelter them—if they had not this backing it is unlikely that design and radiological advances would have moved forward at the pace that they have done. The film manufacturers, on the other hand, who are also the manufacturers of conventional photographic films, make their major profits from the sale of X-ray film and employ the major part of their staffs on its production. My assessment of the number of persons employed in the manufacture of X-ray apparatus, of X-ray tubes and other accessories, of X-ray film, of distribution and installation and maintenance in Great Britain is slightly under 10,000. Together with the figures I have already given, that means that probably somewhere in the region of 20,000 persons are employed one way or another in the realm of X-ray work, and that the cost transferred to the population either by the Exchequer or by industry is somewhere in the region of £29,000,000 or £30,000,000 per annum.

I do want to consider briefly the *saving* and *advantages* that this has brought to our way of life. Many of them are intangibles. Some are hard business facts. In medicine, health preserved, health restored are not factors that can be measured. Reduced patient/days in hospital mean hospital beds available for more people. Earlier return to work means less dislocation of that work and reduced domestic upset if wages are involved. These facts are all of social significance. To all this X-rays have contributed.

In industry costly procedures are not undertaken if they do not bear fruit. The early detection of defects in design cuts down production costs and increases productivity. Another factor here is the maintenance of safety levels in such things as high pressure boilers, aircraft, and railway engines. Government contracts for aircraft insist on a very high level of X-ray inspection throughout and quite apart from moral issues or business grounds, or Government demands, the insurance companies have realized that there is an actuarial significance not to be ignored. Again to all this progress X-rays have contributed much.

DANGERS OF X-RAYS

R. W. Emerson in his essay on the Law of Compensation expounded that for every peak there is a corresponding trough and for every good a corresponding bad. X-rays, which have their contribution to make to our way of life, are not without a compensatory bad. X-rays are dangerous to life. This has been learned the hard way. Men

have been maimed and have even lost their lives due to exposure to X-rays. We believe now that we know something of the extent of the danger and how to prevent these effects. Briefly there are three types of harmful effects which may arise: These are direct injury, such as burns or necrosis; secondly as a late result of excessive dose, either at one time or spread over a period, cancer may be caused; the commonest form of this so to be caused is leukaemia. Thirdly genetic mutations may be caused in the germ cells in the reproductive organs; these will not affect the individual concerned, but may manifest themselves in subsequent generations, in the progeny of the exposed individual.

The Medical Research Council has published in the last few years a series of reports showing what it considers to be safe limits of ionizing radiations, of which X-rays are one form. The basic principle is that nobody should ever be irradiated unnecessarily, but that provided certain precautions are observed, and provided there are proper indications for the exposure, there is a range of safety within which to work and within which the advantages that may accrue to the individual far outweigh the possible dangers. As a single example of this, let me tell you the significance of the dose received during X-ray examinations of the chest. It is considered that during life no person should receive a total body dose greater than 200r (the unit of measurement)—remembering that dosage does not wear off, it is accumulated by the individual; it is also considered that no individual should receive a dose to the reproductive organs greater than 50r during reproductive life. In a chest X-ray examination the individual receives a skin dose (and remember this is not a total body dose) of about 1r (and his permissible dose is 200r total body); and at the same time he receives by scattered rays a dose to the reproductive organs of about 0·1mr (i.e. a tenth of a thousandth of 1r, when his permissible dose is 50r). I think those figures put the matter into proper perspective.

SUMMARY

I have endeavoured to show where X-rays impinge on our daily lives. In this country from the time we get up in the morning until we go to bed at night, there are very few aspects of our lives which have not been influenced by X-rays. The electricity supply for your razor, the printing press for your morning paper, the tyres on the car or bus that takes you to work and the petrol that drives it along, the nylon for your dress or your shirt, chromium in your towel rail, the aircraft that brings your overseas mail, the construction of your telephone, the ink in your pen, the sausage you have for lunch or the chocolate you eat afterwards, the fluorescent lighting in your office, criminal investigations in the community, the cost of the articles you buy, the taxes you pay, your health, possibly your death, the components of your refrigerator, the paint on your house, the pearls you gave your wife, the sponge you wash yourself with—all this and much more may be influenced in twentieth century Great Britain by X-rays. Now in the few minutes left to me I want to revert to the past. All that I have told you tonight stems from the discovery of X-rays by Professor William Conrad Rontgen, Professor of Physics in Wurzburg in Germany on 8th November 1895 (64 years ago). In the following seven weeks by intense effort and work he investigated the properties of these rays remarkably fully. He was a scientist and was interested only in the academic investigation of the phenomenon he had discovered, not in its application. In the course of his investigations he discovered the photographic properties of X-rays and among the photographs that he personally made there were two—Mrs. Rontgen's hand and his shot gun—anticipating curiously the applications, medical and industrial, that I have described to you tonight and which are now used so extensively. He published his findings on the 1st January 1896.

This annual lecture is in memory of Dr. Edward Long Fox, citizen of Bristol and respected physician. He was born in 1832 and practised medicine in this city until the time of his death in 1902. Professor Rontgen's discovery of X-rays was put to

immediate use in medicine, and by the end of 1896 was an accepted if then rather dangerous tool. The last six years of Dr. Long Fox's life was thus in the period of early development of X-rays. In the medical records of Bristol which I have searched there are many references to their use. But in a thorough search of the records of Dr. Long Fox, I can find no reference to his using them.

NEPHROTIC SYNDROME WITH STEATORRHOEA

A Clinical Pathological Conference of the University of Bristol Medical School on 2nd February, 1960

P.M.F. 273/59

CHAIRMAN: PROFESSOR T. F. HEWER

Mr. K. D. J. Vowles: This is the case of a 56-year-old unmarried Irishwoman, who was a cleaner and lived with her niece. She consulted her family doctor in August, 1959, because she had diarrhoea for two days, then two days of normal bowel habit, and then diarrhoea which was unremitting for five or six weeks. Her diarrhoea consisted of three or four loose, watery motions a day with an occasional drop of blood. Her family doctor sent her to Professor Milnes Walker's out-patients, here there was very little to be found on physical examination apart from a slightly distended and noisy abdomen. She was an extremely apprehensive woman, and the Professor felt that although the next step should be a sigmoidoscopy, this would have to be done in hospital under general anaesthesia. She was put on the waiting list for admission, and a barium enema was arranged meanwhile. This was reported as normal, though it did appear that the colon throughout its length had lost some of its normal distensibility.

She was admitted on 30th September, by which time she had had diarrhoea for six weeks and had lost 6 lb. in weight. She had no appetite and said that the had become increasingly nervy. On admission we saw a rather frightened, slightly wasted, pale woman. We were able to make out very little by ordinary physical examination: the abdomen was still slightly distended and rather noisy; rectal examination was negative. We didn't discover very much else except that she had a persistent tachycardia of 90 to 100 a minute, and during her ten days stay in this hospital she was midly febrile for most of the time. Two days after she came in I did a sigmoidoscopy under light general anaesthesia. I saw a normal anus, and a rectum which was rather pink and injected, and bled slightly when touched with the sigmoidoscope or a swab. There were no ulcers, there was no pus, and there appeared to be no mucus coming down from the bowel. I am afraid I have no very clear recollection of the character of the stool, if we saw any on that occasion; I certainly didn't make a note about it.

We felt that here was a woman in the older age group who was developing mild and unexplained ulcerative colitis, and that she should have medical treatment. Because we knew of Dr. Naish's special interest in the condition the Professor decided to consult him about her further care. At just about this time the house surgeon noticed that her blood pressure was persistently low, with a systolic pressure of 90 mm of mercury, and in view of this and of her tachycardia and continued diarrhoea we did her serum electrolytes and a blood count. Her haemoglobin was 71 per cent; her white count was 7,300, with a normal distribution of cells; her sedimentation rate was 80 mm in one hour and her serum electrolytes showed a normal sodium, a low potassium (2·65 mEq/Litre) and a low chloride (95 mEq/Litre); the serum protein also was low, the total being only 4·7 g per 100 mls. We felt that all these figures were adequately explained by her diarrhoea and by the condition we had seen on sigmoidoscopy. We started her on potassium supplements in the form of potassium citrate by mouth, and at that stage Dr. Naish saw her and took her to Frenchay Hospital for further investigation.

Dr. Naish: I was rather puzzled by this woman when I saw her at the Royal Infirmary. I didn't feel that she could be a straightforward case of ulcerative colitis

for a number of reasons. Firstly, she had become ill so very quickly. Secondly, she had a very low serum potassium, which is unusual in a person who is only passing five or six motions a day, though extreme potassium loss may occur in people with much more severe diarrhoea. The third point was that she had some soft oedema of the ankles; I concluded that this oedema was due to protein loss because there was no evidence of heart failure, but I thought it unlikely that her diarrhoea was sufficient to cause hypoproteinaemia. The final point was that she had some finger clubbing, which I tend to associate with wasting disorders of small intestinal origin. Her abdomen was tumid, distended and gurgly on palpation. The whole clinical picutre looked to me more like a sprue syndrome than ulcerative colitis. On the other hand the occult blood test on the stools was positive, and Mr. Vowles had seen this rather red, granular mucosa in the rectum. I must confess that I was very puzzled as to the diagnosis: like many clinicians who can't make up their minds at once I decided to see more of the patient and think about her, and that is why she was transferred to Frenchay Hospital.

But it wasn't at all easy, even after further thought and investigation. We started by studying the protein metabolism, and we were rather staggered to find that her total serum proteins were down to 3·62 g per 100 ml and the albumin to the astonishingly low level of 0·146 g per 100 ml. I had noticed on the chart at the B.R.I. that albumin had been found in her urine on at least one occasion, and on checking this we found that she was excreting in her urine up to 10 g of protein a day. (Dr. Eastham will tell us something more of the detail of these biochemical investigations.) On sigmoidoscopy I noticed the same redness and granularity of the mucosa as was found by Mr. Vowles, but I was also able to see the stool coming down from above, and it was quite clearly fatty. One often finds a red, granular rectal mucosa in patients who are suffering from diarrhoea due to steatorrhoea; I presume that it is due to irritation of the mucosa by fatty acids. We found then that on a normal ward diet she was excreting an average of 9 g of fat a day, which is well above the normal figure. She had an anaemia, with a haemoglobin of 55 per cent and poor haemoglobinisation of the red cells. She was losing potassium in the urine as well as in the stools, and her serum potassium fell as soon as she was taken off her very high potassium diet. We reduced her potassium supplements for a short time, but only because Dr. McGowan, who was carrying out some special tests on her, asked us to do so.

So here was a lady who had become ill very rapidly, who had evidence of a malabsorption state and steatorrhoea, who was losing protein through her kidneys at quite a rapid rate, and whose serum albumin had fallen very low. This was a difficult thing to fit together, so we asked the radiologists if they could help us. We had in mind the possibility of a fistula between the small and large intestines, due to perforation of a diverticulum or perhaps through a small neoplasm between the two structures, since severe protein loss can occur in this condition. Dr. Gaskell accordingly made barium studies of the small intestine, about which he will tell you presently. The rest of her story was short. We tried to put protein into her intravenously as triple-strength plasma, but we found that the patient was losing protein from the bowel and kidney so fast that we just couldn't keep up with it; it was like trying to fill up a bath with a small cup when the plug is out. She had intravenous protein therapy for five days, but as we couldn't keep pace with the tremendous protein loss she weakened and finally died in a hypoproteinaemic state.

Dr. Gaskell: We have two lots of X-rays of this lady. The first examination was of the large intestine, carried out at the B.R.I. This did not show any special abnormality, but the radiologist conducting the examination noted that the calibre of the pelvic colon remaind rather narrow during the barium filling, which presumably signified an increase in tone. The films showed a normal colonic outline otherwise, and excluded the possibility of any fistulous connection with the small intestine. There was slight reflux through a rather incompetent ileo-caecal valve.

The second examination was conducted when the lady came to Frenchay and we were asked to do small intestine studies of her. Time did not allow us to start at the duodenum in this particular case, and we first saw her after she had been given half a cup of non-flocculable barium in the ward. Thereafter films at intervals showed rapid transit and dilution of the opaque material. Three hours after her meal there was segmentation of the barium, which had clumped into lumps, a feature indicating the presence of mucus. There was also a coarsening of the mucosal pattern, indicating swelling of the mucosa, which is generally due to oedema. The four hour film showed barium filling the large intestine round to the rectum; the transit was thus quite abnormally rapid.

What conclusions can we draw from this? Firstly, that there was a mucus-containing intestine showing abnormal structure and function, an appearance seen in steatorrhoea of the young or elderly and in tropical sprue, conditions described together for convenience under the heading of the malabsorption syndrome. Secondly, that there was no internal fistula to account for the diarrhoea.

Finally, a chest film was taken. From it you could see that the heart was displaced to the left, and a further density was visible through the heart shadow, which was reported as a collapsed left lower lobe. A second, more penetrating film did not define the area fully, but we assumed that the left lower lobe was indeed collapsed by some underlying disease of so far uncertain nature.

Dr. Naish: The lady had a loose cough which became worse during the fortnight or so she was at Frenchay, and we found a little dullness at the left base. I looked at these films and thought that possibly some of the opacity was due to fluid accumulating as part of her generalized anasarca.

Dr. Eastham: You have heard about the steatorrhoea. The upper limit of normal fat excretion in the stool, expressed as fatty acid, is 5 g per day, and she was excreting between 9 and 10 g per day, averaged over a period of three days.

She also had persistent proteinuria. Here (Fig. 1a) is the protein electrophoretic pattern of a normal serum. If you compare with this the pattern demonstrated in this patient's serum (Fig. 1c) you will observe the gross derangement, and in particular the complete absence of albumen. If now you compare the electrophoretic pattern of the patient's *urine* (Fig. 1b) with that of normal *serum* (Fig. 1a) a close resemblance is immediately obvious. This sample of urine was obtained after the patient had had a transfusion of double strength plasma. There was thus no doubt that we were dealing here with a nephrotic syndrome, whatever else might be there as well.

In an attempt to piece together the steatorrhoea and the nephrosis Dr. Naish suggested the possibility of lupus erythematosus or some other collagen disease. We examined the blood for LE cells without success, however.

There is not much more to say, except that over a five day period she lost about 10 g of protein each day in her urine. At the same time, over a ten-day period she received 22 bottles of plasma, equivalent to more than 500 g of protein. Since she remained grossly hypoproteinaemic despite this, with a serum protein level of about 3·6 g per 100 mls, it is evident that the kidneys were not the only route by which she was losing protein. It seems probable that the additional loss was via the alimentary tract.

It is perhaps worth mentioning that in addition to her total serum proteins of 3·6 g per 100 mls, the plasma contained 1·5 g of fibrinogen per 100 mls. Such high levels of fibrinogen occur in nephrosis.

Dr. Naish: A gram and a half is a fantastically high level.

Dr. Eastham: We noticed it at once because when the serum was sent for analysis it contained a large fibrin strand. Curiously enough the serum was not lactescent: in the nephrotic syndrome associated with glomerulonephritis the serum is usually milky, but this one was not.

Dr. Naish: Did you say anything about potassium loss?

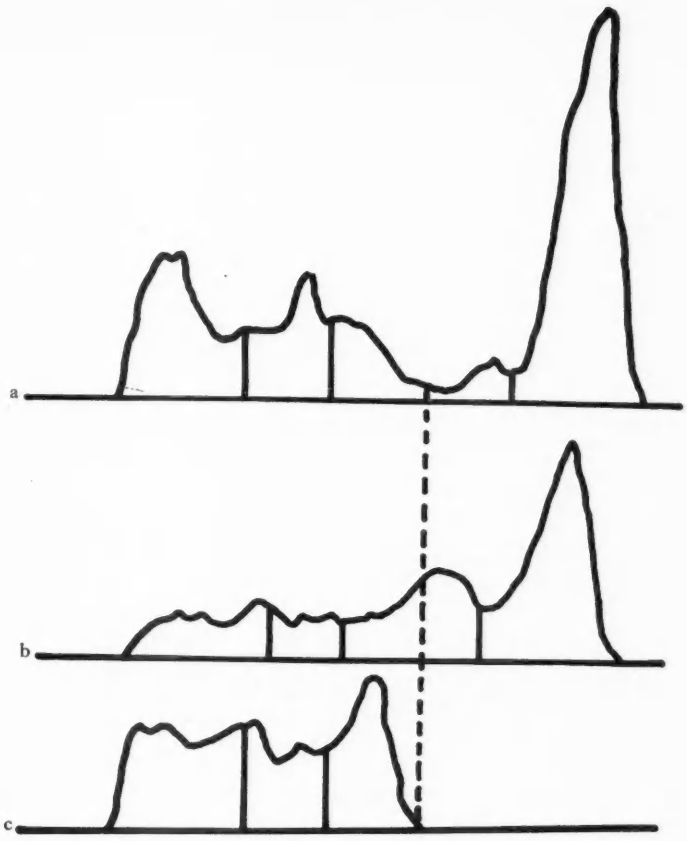


FIG. 1

(a) *Normal serum protein electropheresis pattern.*
(b) *Patient's urine protein electrophoresis pattern after plasma transfusion.*
(*Note similarity to* 1 (a)).
(c) *Patient's serum protein electrophoresis pattern.*
(*Note absence of alpha−1 globulin and albumin*).

Dr. Eastham: On the few occasions when we estimated it we did not find much loss in the urine: the levels were of the order of 1 to 2 g per day, well within the normal range of up to 5 g per day. Since the serum potassium level tended to fall when she was taken off her high potassium diet one can only assume as you suggested, that it was being lost from the bowel.

Professor Perry: We were told originally that the albuminuria was inconstant. I was going to ask whether it became permanent, but it is obvious from what we have just heard that it did. With regard to the potassium loss, I believe that there is a syndrome in which such severe losses do occur from the intestine. Could Dr. Naish tell us whether the liver or spleen became enlarged?

Dr. Naish: The liver and spleen were never enlarged enough for us to feel them. Regarding the potassium loss from the intestine, this may of course be very great if there is diarrhoea originating high up in the intestine, as for instance in chronic pancreatitis or with a fistula between the large and small intestines. Even in ordinary adult coeliac disease you get quite a tendency to potassium depletion. It is quite uncommon, I think, in chronic ulcerative colitis unless there is terrific diarrhoea. There is of course a special syndrome of potassium loss associated with a papilliferous tumour of the colon.

Professor Perry: One other thing: is it really fair to assume that there must be some other protein loss, other than in the urine, if despite fairly massive plasma transfusion you can't raise the plasma proteins? My experience in cases of what I regard as perfectly simple, honest-to-goodness nephrosis is that this is just what happens. I have tried with three or four times concentrated plasma to raise their plasma proteins, but with little success, and I haven't been able to account for all of it in the urine. I have a feeling that there is somewhere in the body where you store protein, and that when that store is depleted you make it up first; but I'm afraid that it is just an idea. I wondered whether it was fair to say that because her blood protein failed to rise despite these plasma transfusions the protein given to her must have been lost.

Dr. Naish: It wasn't only for that reason. It was rather because the proteins had fallen so fantastically low in such a short time, and because we knew that she had a malabsorption state, that we thought it most likely that she was losing protein via the intestine as well.

Professor Perry: She was not absorbing her protein either, was she?

Dr. Naish: No, that's quite true. But attention has been focussed in recent years on the possibility that you can lose vast quantities of protein from the gastro-intestinal tract. It can happen with hypertrophic gastritis and in certain of the sprue syndromes.

Might I try to answer the question you asked earlier about the intermittency of the protein loss in the urine? I can't say anything about her state when she was in the B.R.I. because I have no charts. For the first two days after she came over to Frenchay the position is uncertain, but after we started looking for albuminuria regularly it was there all the time.

Professor Perry: I am really wondering whether something developed on top of her malabsorption syndrome which might have given rise to the massive albuminuri before she died.

Dr. Naish: It certainly looked like that.

Professor Perry: That was why I asked you about the liver and spleen.

Dr. Eastham: This table (Fig. 2) gives you briefly the percentages of albumin in the urine about the time when the intensive plasma transfusions were started. Before the transfusions no albumin could be detected in the urine, but after the transfusions

FIG. 2

DATE	URINE	
	Total protein	*Albumin*
30–31/10/59	7·22 g	nil
31/10–1/11/59	6·28 g	nil
	Plasma transfusion started (4 bottles per day).	
1–2/11/59	8·59 g	19·3%
2–3/11/59	14·5 g	41·9%
3–4/11/59	11·5 g	48·5%
5–6/11/59	aliquot only received	60·0%

began the percentage of albumin in the urine rose steadily. I quite agree that we have not explained where all the protein was going. In the nephrotic syndrome the oedema fluid may increase the potential fluid volume into which the protein can pass from, shall we say, 3–5 litres to about 11 litres. Even so, after 22 bottles of plasma there are 500 g of protein to be explained away, and we have only accounted for about 40 g.

Professor Hewer: Could Dr. Naish tell us something about clubbing of the fingers in association with lesions of the small intestine?

Dr. Naish: People with adult coeliac disease, or non-tropical sprue, often have finger-clubbing, and they are a bit pigmented. It is quite a characteristic appearance, though not all such patients have it.

Dr. Wright: If I may add one small piece of information, I measured her total body potassium on three occasions. In spite of the fact that she had massive doses of potassium all the time she was in the B.R.I. and in Frenchay the total potassium fell throughout, and was in fact lower just before her death than when she was first seen.

Dr. Naish: The diseases which we considered as possibilities here, since they can cause both the disorder of the small intestine and the derangement of renal function, were disseminated lupus erythematosus (for which we could find no evidence at all) and amyloidosis. I should perhaps explain that this is one of the reasons why this desperately ill patient got away without any treatment with corticosteroids: they are said to make things worse in amyloidosis. It was really difficult to stand by and watch this lady just wastlng away, and to be able to do nothing for her except pour plasma in, and even this was eventually abandoned when it became clear that we could not help her.

Professor Hewer: Was there anything abnormal in the cellular content of the stools?

Dr. Naish: We usually ask for a wet film of the faeces to be examined to determine whether there is any excess of fatty acid crystals (typical of amlabsorption syndrome) or oil globules and meat fibres as in chronic pancreatitis. I can't find any record of such an examination in this case, I'm afraid.

Dr. Sandry: I had some warning of the complexities of this case before I was actually called into consultation, so to speak; the patient was a major topic of conversation in the laboratory for about a fortnight before she died. When I did eventually see her I found her to be a wasted woman, with slight oedema of the sacral tissues but none elsewhere. The serous cavities were moist, but not excessively so. The heart was small, weighing only 180 grammes: it showed some dilatation of the right and left ventricles but no other abnormality. The blood vessels were healthy, with one exception which I will mention presently. The kidneys were swollen, the left weighing 180 grammes and the right 185 grammes. Externally they appeared smooth and pale, the capsule stripping quite easily from each. The cut surfaces were pale, the pallor being evident principally in the cortex, which bulged somewhat. Having hear rumours of amyloidosis as well as simple honest-to-goodness nephrosis (a condition mentioned by an earlier speaker, which I do not personally recognize) I looked particularly carefully at the kidneys: it seemed to me that they did not present the picture of amyloidosis at all, the soft, bulging cut surface being quite unlike the waxy pallor of amyloidosis. The renal pelves, ureters and bladder were quite healthy. One tributary of the right renal vein in the upper pole of the kidney was partly occluded by mural thrombus; that part of the kidney did not appear any different from the rest, and I could not believe that the thrombus had really had any great effect on the circulation through it. The adrenals were slightly nodular and a little swollen, and showed some loss of cortical lipoid. The spleen also was rather swollen, weighing 195 grammes; it looked very engorged, with a rather softened pulp and possibly a little hyperplasia of the Malpighian bodies. The soft cut surface bulged slightly, and again did not present the appearance of amyloidosis at all. The liver was enlarged, weighing 2,050 grammes. To the naked eye it showed acute venous congestion with probably a good deal of fatty change; it had a rather greasy cut surface, but again not

the waxy pallor of amyloid infiltration. The gall bladder and bile ducts were healthy and the pancreas appeared to the naked eye quite normal.

Turning now to the alimentary tract, the oesphagus and stomach appeared quite normal. The duodenum showed a little patchy mucosal congestion but nothing more. The small intestine also showed a little mucosal congestion, but in the autopsy room the mucosal pattern appeared quite normal; the contents were dark, greyish-brown and fluid. The caecum and appendix looked healthy. The colon appeared slightly thickened, its wall a little oedematous and its mucosal surface rather granular in appearance, but I could see no ulceration. The rectum was healthy. A few calcified mesenteric lymph nodes represented a healed abdominal primary tuberculous complex.

The right lung was congested and oedematous. In the lower lobe of the left lung (which had been the subject of a certain amount of speculation clinically) there was a large growth, 9·5 cm in diameter (Plate XIII). It occupied the basal segments of the lower lobe, and the main lower lobe bronchus ran into its centre. I found no metastases anywhere in the body. This tumour must I suppose have been hiding behind the (very small) heart. I found no change in the central nervous system.

I emerged from the autopsy room having decided that this was not a case of amyloidosis, but supposing that it must be nephrosis, though whether it was simple, honest-to-goodness nephrosis I could not say. The first histological section, available a few days later, gave me no surprise: it showed the pulmonary tumour to be a rather poorly differentiated squamous carcinoma, extensively necrotic but without much in the way of inflammatory changes superimposed upon the necrosis. When I examined the first sections of the kidneys, however, I was mortified to discover that this was in fact a typical and severe example of amyloidosis. Here (Plate XIV) are two glomeruli, showing amyloid deposition in the capillary tufts. Amyloid was also present beneath the basement membranes of many of the tubules, in the interstitial tissue throughout the cortex, and in the medulla as well. There was a little material giving the staining reactions of amyloid actually in some of the tubular epithelial cells, which throughout the whole kidney appeared rather flattened and degenerate. There was even similar material in the lumina of some of the tubules. The thrombus in the tributary of the right renal vein showed some organization and had evidently been present for some little time. The spleen showed amyloidosis of the nodular type; of course, on looking back at the fixed specimen I was able clearly to see the Malpighian bodies with their amyloid, greyish in colour, sago grains if you like that sort of thing. The liver contained a lot of fat and a very little amyloid, and showed considerable acute venous congestion: its enlargement appears to have been due principally to fatty change and acute congestion, and not to amyloidosis. As regards the other organs, the adrenals showed considerable though patchy amyloid deposition, chiefly between the cords of cortical cells in the zone fasciculata. The pancreas contained no obvious amyloid and showed no evidence of pancreatitis. The thyroid showed quite considerable amyloid deposition, a good deal of colloid storage and some scarring. The single parathyroid I examined contained a trace of amyloid only, not enough to alter its structure. The pituitary contained no amyloid, and I could not demonstrate amyloid in the myocardium.

I had hoped that study of the alimentary tract might be quite informative as the autopsy was only eight hours after death, but unfortunately there was considerable autolysis throughout the intestine. However, although the amyloid change is not striking, on close study one can see that there is in fact widespread deposition beneath the endothelium of the small blood vessels. I have examined sections from about a dozen different levels in the alimentary tract; there is some variation in amount at different levels, but there is obviously a great deal of amyloid present. There is a little lymphocytic and plasma cell infiltration in the submucosa and lamina propria mucosae of the small and large intestines, but I cannot see any actual ulceration. Accurate assessment of the degree of mucosal damage is impossible because of the severity of the

autolysis: the clinical symptoms of persistent diarrhoea and the derangement of fat absorption suggest that there was a considerable functional disorder.

In summary, therefore, this turned out to be a case of severe amyloidosis, affecting principally the kidneys, spleen and alimentary tract, and associated with a bronchial carcinoma (you could perhaps call it an occult bronchial carcinoma), certainly necrotic but not apparently severely infected. The clinical presentation of the case seems to me to have been remarkable for several reasons, outstanding among which I find the acuteness of the onset of the initial symptom of diarrhoea, the steatorrhoea and the extraordinarily gross protein loss, particularly through the kidneys. This is not the time for a lecture on amyloidosis, so I will leave the matter there for discussion.

Professor Hewer: I don't suppose you examined the tongue for amyloid, did you?

Dr. Sandry: I don't know, sir, why you should say that you don't suppose I examined the tongue! You are quite right, of course, I didn't. It is one of the major deficiencies of my examination. I did examine the heart muscle, but I did not examine the tongue or the subcutaneous tissue. I would like to have examined the bone marrow: in fact, I shall do so, as I have recently found a fragment among the specimens, but I don't really think there is any possibility of myelomatosis in this case.

Professor Hewer: I expressed my question like that because I thought that as amyloidosis was only divulged to you later, it would have been very surprising if you had taken a section at the time.

Professor Perry: I am not clear whether this is put forward as a case of generalized amyloidosis secondary to a carcinoma of the bronchus, or as a case of primary amyloidosis with a coincidental carcinoma of the bronchus, or as a case of malabsorption syndrome and secondary amyloidosis with an incidental carcinoma of the bronchus.

Dr. Sandry: Of course I knew that somebody would ask this question. When I saw Professor Perry come into the room just now I had a shrewd idea who it would be. I personally would say that this should be regarded as a case of secondary amyloidosis in association with a bronchial carcinoma. I do not know how the carcinoma acted as an aetiological agent, but I do not think that anyone knows just how any of the recognized aetiological agents acts in producing this disorder. I would say that the malabsorption syndrome and the diarrhoea were secondary phenomena, essentially due to amyloid deposition in the bowel. Diarrhoea is a recognized, though not I think a very common symptom of amyloidosis. In regard to the steatorrhoea, I wonder in how many cases of diarrhoea due to amyloidosis the fat content of the stools has been estimated. I don't know whether steatorrhoea would be found commonly if this were done; it has been recorded, I think: in fact I'm sure it has. With regard to the distinction between primary and secondary amyloidosis, my impression, from an admittedly rather sketchy reading of the literature, is that there is a growing tendency to insist less upon the distinction between the two conditions nowadays. As Professor Symmers says in a recent article, although in amyloidosis without any obvious cause (commonly called primary) the substance tends to be distributed chiefly in the connective tissues rather than in the parenchymatous organs, and the reverse is true of amyloidosis in which an acceptable cause can be found (commonly called secondary), nevertheless one may find a typical "primary" distribution in a case with an obvious predisposing factor, and vice versa. It is in fact quite common to find severe involvement of the kidneys, spleen and liver in the so-called primary type of amyloidosis.

Professor Hewer: Yes, that is exactly what Symmers said. On the whole one expects to see the tongue and heart involved in the primary type, but it is not necessarily so. The albuminuria, of course, is not surprising in severe amyloid kidney; this was quite a severe grade of amyloid kidney, wasn't it?

Dr. Sandry: Yes.

Professor Hewer: All the glomeruli were very much involved. The nephrotic syndrome is a not infrequent result of amyloid kidney, and she was obviously losing

a tremendous amount of albumin at the time, partly because of the amyloid kidneys. Having achieved a very low plasma albumin one would have expected her to develop a very high level of lipid in the blood.

Dr. Sandry: Yes, but in fact this did not appear to be so.

Professor Hewer: She was losing a great deal of albumin by some route which was not determined, more than could be accounted for by the renal leakage. It must undoubtedly have been escaping from the gut, in which there was severe amyloidosis. I wonder whether lipid could have been escaping as quickly as albumin was, from the gut.

Dr. Eastham: I don't know any actual work on faeces which has shown the pattern of the protein loss.

Dr. Naish: With regard to the frequency of steatorrhoea in amyloidosis, the association is well recognized, and one does occasionally come across a patient with a steatorrhoea syndrome who has amyloidosis of the small intestine and nowhere else. I remember an old chap at Snowdon Road who had steatorrhoea of uncertain origin. He was passing "aluminium-paint" stools. For a very long time we couldn't explain this state, but when he died the post-mortem examination revealed amyloidosis confined entirely to the small intestine. Another case I can call to mind was a patient who had tuberculosis and developed Addison's disease. We treated her with small doses of cortisone for two or three years, but finally she fell ill with diarrhoea and wasting and eventually died. The autopsy revealed amyloidosis not only of the intestine but also of the adrenals, and this was presumably the cause of her Addison's disease.

Professor Hewer: I probably missed this point in the biochemical story, but was her dietary fat intake measured, and if so was there any relation between this and the fat output in the stools?

Dr. Naish: No, this was not done. I should say that the lady was taking well under the average ward diet, which contains about 70 g of fat a day, for she had a very poor appetite and was very ill. She was losing about 9 g a day, which is not excessive: I have known a patient with acute pancreatitis who was losing up to 70 or 80 g of fat a day, strangely enough on a dietary intake which was less than that. It has been shown that there are fat-producing organisms in the bowel, so that measurement of the dietary fat intake is not very helpful.

Professor Neale: Actually I suppose that the steatorrhoea here, being mild, could have been due entirely to intestinal acceleration. I don't know if you said what the speed of transit through the gut was?

Dr. Gaskell: It was very erratic.

Professor Neale: Was the time factor actually worked out?

Dr. Gaskell: Yes, it was about three hours.

Professor Neale: Surely such a rapid transit fully explains the steatorrhoea, there being no time for absorption.

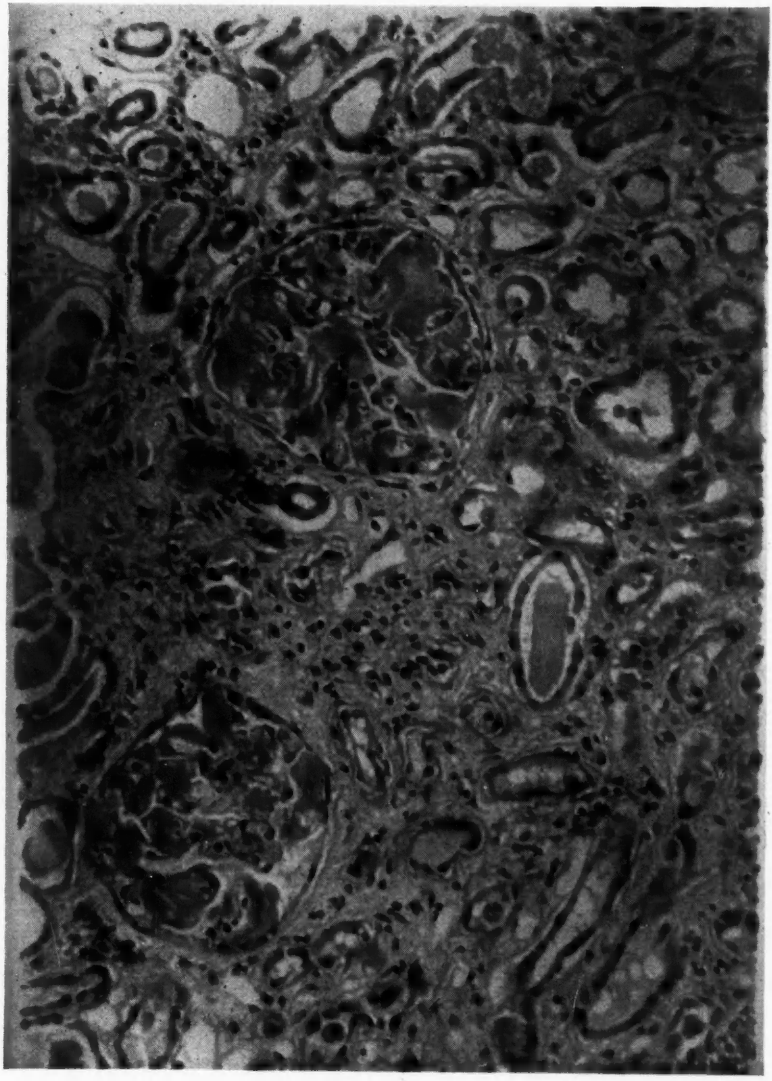
Professor Perry: The absence of lipoid in the serum is interesting. Five years ago some people were saying that the best test for steatorrhoea was to give a patient some fat and have a look at his plasma an hour to an hour and a half afterwards. I believe that this has not proved as satisfactory a test as had been hoped.

Dr. Naish: I know it is rather speculative at this distance, but I would not agree with Professor Neale that the malabsorption here was due purely to hurry through the intestine; I think it was much too severe. I have seen people who run barium through to the colon in about a couple of hours, very nervous characters with gurgly tummies, and they have no malabsorption. I was convinced, personally, that the loss of protein was taking place largely through the bowel, though it was occurring through the kidney as well. She had gone downhill so quickly.

Dr. Gaskell: No questions have been asked so far about the place of sepsis in this

PLATE XIII

PLATE XIV



case. We have not heard much about the blood picture, and Dr. Sandry has not told us how much sepsis there was distal to the growth in the bronchus.

Dr. Sandry: The growth showed a good deal of necrosis, but little evidence of inflammation. It extended to the pleural surface, so that there was little or no lung tissue beyond it in which sepsis due to bronchial obstruction might have occurred. In fact I was not able to demonstrate any severe sepsis anywhere.

Professor Hewer: Of course these squamous cell carcinomas can be very slowly growing. I wonder whether Dr. Gaskell thinks that this one could have been hiding behind the heart at the time of the chest X-ray, or whether it must have increased in size since then.

Dr. Gaskell: I feel certain that the tumour is in fact visible in the X-ray; there is a double density within half a centimeter of the cardiac border, which may be the actual edge of the tumour or the margin of the collapsed lower lobe. Such an abnormal finding is of course ample justification for further investigation.

Professor Neale: Could I ask one simple point? Do the findings in this case throw any light at all on the mechanism by which protein escapes into the urine in nephorsis? Here we have a demonstrable lesion, whereas I believe that in ordinary nephrosis there is very little that can be demonstrated histologically.

Professor Hewer: There are changes in the basement membrane of the glomeruli in such cases.

Professor Neale: Are there any comparable changes in this particular case? The end result is similar, loss of albumin in the urine. Is any light thrown upon the nephrotic albuminuria by the microanatomy (micropathology, if you like)?

Dr. Sandry: In this case, sir, the *ultra*-microanatomy was not studied: I have no access to an electron microscope.

Professor Hewer: I think we shall have to assume that the amyloid is responsible for most of these changes, though we do not really know why the amyloid is there. It is most unusual to find amyloidosis as a complication of a solitary pulmonary neoplasm of this kind.

Professor Neale: One final question. Is there only one type of amyloid material, or are there several different kinds?

Professor Hewer: There are several chemically distinct types.

Professor Neale: Can you establish that by differential staining?

Professor Hewer: The staining reactions show great variability from case to case.

REFERENCE

Symmers, W. St. C. (1956). "Primary amyloidosis: A Review". *J. Clin. Path.*, **9**, 187.

Notes and News

F.R.C.O.G.: Marjorie O. Bennett.

Professor A. V. Neale has been appointed President of the British Paediatric Association.

Professor A. I. Darling, in June, gave an address to the Congress of European Organisation for Research on Fluorine and Dental Caries Prevention.

Dr. Macdonald Critchley gave the centennial oration during the centenary celebrations in June of the National Hospital, Queen Square.

Dr. R. J. A. Berry, formerly Professor of Anatomy and Dean of the Faculty of Medicine, Melbourne University, has been awarded an Emeritus Professorship by the University Council.

Surgeon Captain J. L. S. Coulter has been elected a F.R.C.S.

Examination Results

M.D. Cambridge: Dr. Clifford Evans.
M.D. Glasgow: Dr. J. Sluglett.

UNIVERSITY OF BRISTOL

M.D.

D. H. Bowden
W. K. Metcalf

Ph.D.

Dinah Payne

D.P.H.

Addis, S.
Blancarte, J.
Brzezinski, Z. J.
Ducksbury, Christina F. J.
Mair, Marjorie
McGregor, C. M.
Osman, I. O.
Taylor, R. Y.

M.B., Ch.B.

WITH SECOND CLASS HONOURS

Draisey, T. F.
Ferguson, D. R. (*with Distinction in Surgery*).
Marsh, Margaret E. (*with Distinction in Public Health*).
Morley, Jean L. (*with Distinction in Public Health*).
Morris, Barbara, M.
Neale, G. (*with Distinction in Child Health, and in Public Health*).
Stentiford, N. H.

PASS

Beddard, J. B.
Beesley, Barbara
Bisson, Margaret J.
Bisson, P. G.
Blandford, A. G.
Clarke, R. J.
Cottrill, P. H.
Critchley, Sheila A.
Daniel, A. R.
Dash, J. R.
Dyall, C.
Flaherty, T. H.
Gay, M. J.
Gorman, B. J.
Gurney, P. W. V.
Hackman, B. W.
Hayward, C. J.
Hinchliffe, A.
Langley, A. G. S.
Malkin, Isobel C.
Miles, Mary P.
Pitman, R. H.
Price, Isabel M.
Rawlins, J. C. D.
Rich, W. J. C. C.
Sebire, J. N.
Taylor, P. H.
Warnecke, D. P.
Whatley, R. J.
White, D. M. D.
Williams, B. E. O.
Winslade, J. R.

Prizes

The Edgeworth Prize: P. Breddy.
The Edward Fawcett Prize: Miss G. M. Duffin.
The Foyle Prize: D. J. Moffatt.
The Mackie Pathology Prize: Mrs. B. M. Morris.
The Richard Clarke Prize: G. Neale and Miss J. Morley.

Appointments

Dr. A. E. Read has been appointed Lecturer in Medicine, University of Bristol.

Dr. T. E. Oppé has been appointed Assistant Director of the Paediatric Unit, St. Mary's Hospital, London.

P. O. Nicholas, M.B. (Bristol), D.C.H., has been appointed Senior Assistant M.O. and School M.O., Castleford and Normanton, Yorkshire.

UNITED BRISTOL HOSPITALS

February–June, 1960

Name	*Appointment*	*Formerly*
READ, A. E., M.D.(LOND.), M.R.C.P.(LOND.).	Assistant Physician (Hon. Contract) in the United Bristol Hospitals during tenure of the post of Lecturer in Medicine in the University of Bristol.	Senior Medical Registrar and Tutor in Medicine, Postgraduate Medical School of London and Hammersmith Hospital.
OPPÉ, T. E., M.B., B.S. (LOND.), M.R.C.P., D.C.H.	Assistant Paediatrician (Hon. Contract) in the United Bristol Hospitals during tenure of the post of Lecturer in Child Health in the University of Bristol.	Lecturer in Child Health, University of Bristol. (Hon. Contract, Senior Registrar status in the United Bristol Hospitals.)
BERRY, D. C., M.D.S.	Assistant Dental Surgeon (Hon. Contract) in the United Bristol Hospitals during tenure of the post of Lecturer in Prosthetics and Dental Surgery in the University of Bristol.	Lecturer in Prosthetics and Dental Surgery in the University of Bristol. (Hon. Contract, Senior Registrar status in the United Bristol Hospitals.)
MOBAREK, A. L., M.B., CH.B.(CAIRO), D.M.R.E.	Registrar of Radiotherapy.	Resident at the Radiology Department, Cook County Hospital, U.S.A.

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CLINICAL GENETICS AND THE PRACTITIONER

BY

*THOMAS E. OPPÉ

Lecturer in Child Health, University of Bristol

During the past few years there has been a remarkable increase in interest concerning human genetics. Undoubtedly the main reason for this has been the advances in knowledge that have come at a time when the demand for a new knowledge has been urgent and articulate. The nineteenth and early twentieth centuries will go down in history as the golden age of scientific medicine, marked by an intense preoccupation with the external causes of disease. Bacteriology disclosed the bacterial and viral agents causing infective disease, nutritional science revealed the role of the vitamins and other nutritional elements in the causation of deprivation syndromes. Cancer research was much occupied with chronic irritants from spindle-oil to smegma, and "imferon" to cigarettes.

The result was a depersonalized, scientific medicine which elucidated most of the diseases due to infection, malnutrition and other external agents, leaving the degenerative diseases and neoplasia as a hard and unsolved core. The science was good, the depersonalization was bad. The individual, encouraged by the psychiatrists, the geneticists and the Welfare State, has risen again to assert his rights. Why do some smokers get cancer and others not, why do only a minority of children who have had a streptococcal infection get rheumatic fever or acute glomerular nephritis, why do some slothful, gluttonous business executives have coronary artery disease while others equally indolent and gluttonous do not? Peering at Aschoff nodes, or thrombosed coronaries, or meticulously classifying cells in tumours of the bronchus are unlikely to answer the questions. The geneticist, however, may well have something to contribute.

The year 1945 saw the birth of the atomic age which may lead us to a fearful and obvious calamity; however, even if we escape the full horror of atomic war, there are more subtle ways in which nuclear radiation may be harmful. Ionizing radiations distort and damage dividing cells with hazardous implications for the heredity of man. These dangers have brought into being the new science of radiobiology. This is of immense concern to the geneticist and implicates every doctor who sends a patient for a radiographic investigation.

Just as our new concern is with the essential individuality of our patients, so it is associated with a new outlook towards the essential sameness of the family of mankind. Policies of repression and inequality based upon the alleged genetic inferiorities of Jews or Negroes are being rightly criticised. Advances in genetic knowledge can give us cold, objective facts with which to sweep away emotional prejudices and misconceptions.

There is now almost no field of human activity in which the geneticist is not involved. Even such moral and religious issues as artificial insemination (A.I.D.) have a genetic aspect. No-one would now pretend that the sought-for perfection of the human race can be brought about by eugenic means, or that policies of selective mating or discriminative sterilization would alter profoundly the destiny of man. However, human genetics can no longer be regarded as an amiable hobby pursued by lovers of rare syndromes, or a fanatical cause which promised Utopia in an imperfect world.

* Present address: Paediatric Unit, St. Mary's Hospital London, W.2.

Modern methods of communication, notably the television, have brought these questions and some of the answers into the vision of millions of people. Many of these people have a personal genetic problem for which they will turn to their family doctor for advice. In many cases the doctor will be able to provide wise and authoritative guidance, in others he may feel the need for expert help. The purpose of this article is to review some of the newer work in the field of human clinical genetics in the light of the human problems which have come to our notice at the Bristol Children's Hospital Genetic Clinic. In doing so our main aims have been to put the doctor in the genetic picture and, at the same time, indicate the areas where specialized knowledge may be helpful.

HUMAN GENETIC PROBLEMS

An analysis of the genetic clinic material indicates clearly the type of problems for which patients seek genetic advice.

Premarital problems	4
Whether to have children	2
Whether to have more children	70
Whether pregnancy should be terminated or sterilization is justifiable	8
Whether a condition will be transmitted by their children	5
Doctor or patient interest	13
Reasons not clear	3
	105

In the majority of cases genetic advice is sought after the birth of an abnormal child. The abnormality may be known or merely suspected to be an inherited one, and the parents' concern is whether subsequent children may be abnormal. Rather fewer cases are seen because one or other partner in a marriage or projected marriage is cognisant of some familial disorder and wishes to know the genetic risks of having children. Others who have families containing both normal and abnormal individuals are concerned whether their normal offspring may transmit the disease to future generations. Although usually there is no urgency about genetic advice, sometimes an emergency arises.

Mr. and Mrs. C. 45369

Mr. C. was severely disabled with cerebellar ataxia which he had inherited from his mother. His only daughter was similarly affected and greatly handicapped. When Mrs. C. became pregnant again she was extremely worried that the foetus might be abnormal. As the inheritance is clearly dominant, advice was given that the chances were 1:2 of the child being affected. The anxiety of the mother faced with this poor genetic prognosis was sufficient to justify termination of the pregnancy and subsequent sterilization.

In other cases advice is sought because the family hope for an explanation for the puzzling abnormality, and in some because either the family or the doctor are interested in the genetic aspects of a condition.

The essential facts which the geneticist must have are (*a*) the diagnosis and (*b*) a complete pedigree of the family. It is unfair to expect the geneticist to make diagnoses of obscure cases from the parents' description. Therefore full clinical data are always appreciated concerning all suspected members of the family. Likewise, it is unfair to extract details of family trees often including illegitimacy, consanguinous marriages, etc., from patients unless they are prepared and co-operative. Before referring a case for genetic advice it is helpful if an accurate diagnosis is made, the problem is

clearly defined and the parents are aware of the sort of questions they will be asked and the type of help that they may expect.

Most problems resolve themselves into three main groups:

I The disease in question is not inherited and genetic causes and transmission can be ruled out.

II The disease is inherited and its genetics follows a regular, known pattern of inheritance.

III The disease is familial, and genetic factors are believed to be involved. However, either through the number of genes involved or because of considerable environmental modification of gene influence, no regular pattern of inheritance is discernible.

Although the material at the genetic clinic is highly selected, it is of some interest to see the proportion of patients attending in each of these groups. It should be borne in mind that there is usually some special doubt or difficulty leading to referral in cases of Group I, the non-genetic group. Commonly, this is to provide expert reassurance. In Group II, the diseases definitely and regularly inherited, a good deal of appropriate counselling is done by general practitioners or consultants and there is no need for attendance at a special clinic. It is in Group III, where genetic mechanisms are involved in irregular or obscure fashion that most difficulty arises, and the help of the expert geneticist may be most useful. The genetic clinic does not represent a true cross-section of patients who might be grateful or benefit from genetic advice. A large section is adequately advised elsewhere.

GROUP I. CONDITIONS THOUGHT TO BE NON-GENETIC IN ORIGIN (10 cases)

Cerebral palsy probable due to perinatal trauma or anoxia is the most common in this group, and some cases of mental sub-normality may also be assigned here. Parents of children suffering from leukaemia and other neoplasms, aplastic anaemia and occasional other disorders have been reassured. The problems here is usually a condition which has multiple aetiologies, and separation between those largely caused by heredity and those due to enviromental causes is difficult.

Mr. and Mrs. V. 60560

Mr. and Mrs. V. are first cousins. Their first child was born after a difficult labour ending in traumatic forceps delivery. The child's condition at birth was poor and during the neonatal period he had signs of cerebral haemorrhage. At one year of age he was grossly retarded, small-headed and had a spastic quadriplegia. The diagnosis was cerebral palsy (spastic quadriplegia with mental retardation). The family history was completely negative, except for the consanguinity.

The problem was whether there were genetic risks for future pregnancies. Cerebral palsy may be genetic in origin in some cases, but there is a considerable body of evidence that many cases are caused by perinatal damage to the brain. In this case there was undoubted perinatal trauma, both mechanical and hypoxic. It seemed unnecessary to postulate a genetic cause in addition to an adequate environmental one. A reassuring genetic prognosis was given, and the parents were told that the disease in question was unlikely to be the result of an hereditary taint.

Some rare conditions are seen because their aetiology is quite unknown and the doctor wishes to know whether hereditary factors have been implicated.

Mr. and Mrs. N. 64525

This is a normal, healthy family, except for their third child who was born with all the manifestations of the Moebius syndrome. He had nuclear agenesis (paralyses of the left facial and external rectus nerves), micrognathos, stridor, absent pectoralis major muscles,

absent left nipple, a deformed left hand and dextrocardia. He is making good progress, although he is generally retarded. They had subsequently another child who is quite normal. They were referred to the clinic partly because they were interested in establishing a reason for the malformation and also because of an underlying anxiety that their three normal children might transmit the disease.

Reference to recent literature on the subject showed that there is no obvious familial tendency in this condition, the parents were therefore reassured not only as far as future pregnancies of their own were concerned but also for their children's potential children.

Elimination of important genetic factors, which is the main problem in this group, rests on two main principles. Firstly, that the condition in question is known to have an external causation and the causation was operating in the particular case, and secondly that there is not satisfactory evidence of genetic participation in the condition in question. The latter postulate is difficult to apply. What is satisfactory evidence that genetic inheritance plays a part in the causation of a particular condition? Such evidence may be clinical, gemellological, or experimental.

Clinical evidence is convincing when a condition is clearly shown to be familial and the distribution of affected members of the family follows a regular pattern of Mendelian inheritance. More often it is merely suggestive in that a condition appears in more members of a family than would appear likely by chance. Caution is needed in interpreting such findings. A disease may run in a family because of infection, e.g. tuberculosis, or because of shared environment, e.g. pneumoconiosis in coal-mining families. Complex multi-factorial causative factors may be involved. There is a familial predisposition to coronary thrombosis. This might be due directly to a genetic disturbance in cholesterol metabolism or, much more indirectly, to the fact that over-conscientious, professional families tend to place their offspring in professional or academic careers, or that the eating habits of individuals usually follow by example the dietary habits of their parents.

The study of twinning (gemellology) is a valuable tool. Identical (uniovular) twins have a common genetic inheritance, dissimilar (binovular) twins are no more genetically similar than any sibs. If it can be clearly shown that a characteristic or condition is shown more frequently in identical twins than in dissimilar twins there is a reasonable assumption that the characteristic or condition is determined by heredity. It has recently been pointed out that twins form two per cent of any doctor's practice and there is a tremendous amount to be learned from them (Nance, 1959).

Experimental genetic evidence is difficult to evaluate. Man is unsuitable for genetic experiments owing to his unfortunate habits of marrying for love and producing rather few offspring over a long period of time. Animals or plants which can be selectively mated and produce many generations are more suitable. However, much caution has to be used in interpreting results gained by the study of other species.

Two new approaches to problems of identifying the genetic causation of disease or association with disease are yielding extremely interesting results. The first approach is that of blood group associations with susceptibility to disease. There is no doubt that the blood group of an individual is a genetically inherited characteristic. There are extremely rare exceptions of dissimilar twins sharing blood groups due to foetal inter-placental transfusion; however, these blood group chimeras are statistically negligible. If it can be shown that a disease is consistently associated with the possession of one or other blood group it is reasonable to assume that there may be some genetic factors in that disease. So far, blood group associations have been most firmly established with disorders of the upper alimentary tract, duodenal ulceration, gastric carcinoma and Addisonian (pernicious) anaemia (Roberts, 1959a). Further work in this field must be laborious and involve the statistical correlation of many thousands of individuals whose blood groups are known and who suffer from diseases suspected of being linked to blood groups.

Another recent and important advance is the direct demonstration of chromosome abnormalities in man. New methods of tissue culture and the staining of dividing cells made it possible for Tjio and Lefan in Sweden and Ford and Hamerton (1956) in Britain to identify and differentiate the chromosomes in man. The first result was to show that the normal number of chromosomes in human body cells was forty-six, not forty-eight as had previously been believed. Extension of this showed that some pathological conditions were clearly associated with abnormalities in the number of chromosomes. Such a demonstration is proof of a genetic contribution to the disease in question. A fuller discussion of the clinical value of this method will be given below.

GROUP II. CONDITIONS DEFINITELY AND REGULARLY INHERITED (46 cases)

(*a*) Those due to dominant genes: sixteen families (including hereditary spherocytosis, achondroplasia, cranio-facial dysostosis, muscular dystrophy (peroneal and facio-scapulo-humeral types), vitamin D resistant rickets).

(*b*) Those due to recessive genes: eighteen families (including fibrocystic disease of the pancreas, progressive infantile spinal muscular atrophy, gargoylism phenylketonuria).

(*c*) Sex-lined recessive: twelve families (predominantly the coagulation disorders, haemophilia and Christmas disease, and muscular dystrophy of pseudo-hypertrophic type).

Patients seek advice for these conditions, either pre-maritally, before having children, or when they have an affected child. Patients who have not yet had children may either suffer from an inherited disease themselves or be aware of members of the family who are afflicted. Again, it is important to know the diagnosis, to obtain a full family history and to be aware of the known facts concerning the transmission of the disease. Some typical problems have been:

Miss J. D. 36487

She was a student nurse aged 21. Her brother is a known haemophiliac attending the children's hospital. Her maternal grandfather and one of his brothers were thought to be "haemophiliacs". One of her great-grandmother's sisters had a male child who "bled easily". Miss J. D. was engaged to be married and wished to know whether any children she might have were likely to be "haemophiliac".

The diagnosis was clear, true haemophilia in her brother. The family tree was classically distributed for the sex-linked recessive inheritance of haemophilia, which made it most unlikely that her brother was haemophiliac because of a mutant gene. On this evidence alone the genetic prognosis is calculated as follows. It is almost certain that her mother is a carrier, therefore she herself has a fifty-fifty chance of also being one. If she is not, she need have no fears that her offspring will be affected. If she is, then statistically half her daughters will be carriers, and half her sons afflicted with the disease. The most important question is whether or not she is a carrier. In some cases the female carriers of haemophilia can be identified by estimating the level of anti-haemophilic globulin (A.H.G.) in the blood. However, this is by no means consistently lowered in carriers and in Miss J. D.'s case was normal. Follow-up has not been done, but it would be interesting to know whether or not she has limited her family because of the possibility of her being a carrier.

This example is a good one of the necessity for separating the genetic risks from the wider question of whether a couple are advised to have children or not, the latter problem includes moral, religious and financial issues. Some people believe sincerely

that it is wrong to bring into the world children who may be malformed or diseased, others believe it is wrong to interfere with natural reproduction. The geneticist should be entirely objective and generally will give advice only on the genetic risks. However, as a medical practitioner, he may reasonably give further information of a medical nature. In this case, it is reasonable to point out that haemophilia is a disease of variable severity not necessarily incompatible with a normal life and also that advances in treatment may well occur in the near future which will make haemophilia less of a handicap.

Miss C. 65428

This 23-year-old unmarried girl had affronted her family by bearing the child of a U.S. Serviceman, with whom she was much in love. The baby showed unmistakable signs of being affected by progressive infantile spinal muscular atrophy and died when a few months old. The couple were seriously considering marriage, but both wanted children.

The condition is recognized as being due to an autosomal recessive gene. It was explained to the couple that if they married, the chances of further children being affected were one in four. On the other hand, if they did not marry each other but sought other partners, it was extremely unlikely that any of the offspring would be affected. The reason for this is that both must be 'carriers' of the rare gene for this condition and it would be improbable that such a choice of mating should occur again. It was later heard that they had attempted to solve this dilemma by attempting a further pregnancy, still unwed. Presumably if the second child were normal they would get married, if it should be affected they would "call it a day". This eminently practical and enterprising, if immoral, approach could hardly have been suggested by the clinic!

Mr. and Mrs. W. had normal family histories, but their first child died of progressive infantile spinal muscular atrophy. At the clinic it was explained that the chances of future children being affected were one in four. They decided that they would try again and a second child was born. She was also affected and died within a few months. They again attended the clinic having been advised elsewhere that it would be foolish to have another pregnancy. It was again explained that the odds were three to one in favour of having a normal child. With considerable courage they decided to have another child, but at the same time were put in touch with an Adoption agency. Their third child, unfortunately, was affected, but they were able to adopt a baby.

This case emphasies the importance of the parents deciding for themselves how the genetic risk should be interpreted. There is no doubt in this case that their decision to undertake further pregnancies was influenced by the knowledge that the disease was an almost invariably fatal one. It is perhaps natural that parents should accept greater genetic risks when the outcome is either normality or early death, rather than if there is a possibility of chronic handicapping illness in the child.

Most doctors will be familiar with the classical forms of Mendelian inheritance and it is with the conditions showing these regular patterns that the geneticist is on safe ground. Most of these conditions are due to the action of single genes. If the gene exerts such a powerful effect that possession of the gene in unit dose (heterozygous) produces a clinical abnormality we term that a 'dominant' gene. If, however, the gene only produces the clinical effect in double dose (homozygous) it is termed recessive. In the case of recessive genes in single 'dose' (heterozygotes) the presence of the gene may be detectable by special tests (Hsia, 1959). Until recently our knowledge of genes and their action has been based largely on conjecture, by studying their effects. There have, however, been some real advances in knowledge, both of the structure of genes and the ways in which they produce their effects.

The gene is a distinct but very small particle composed of a nucleic acid (D.N.A.) and proteins. The protein part is probably the component that is responsible for the

unique ability of genes to transmit 'genetic' information. The protein part of the particle consists of polypeptide chains which are folded in a specific manner. Each polypeptide chain has a regular sequence of aminoacids along its length. Changes in a gene might then be due to alterations in the amino-acid sequence or to differences in folding of the polypeptide chains. It is only by the continued handing on to reproducing cells of these chemical structures that genetic inheritance can work. It is thus tempting and not too speculative to say that primary gene effects will be found by tracing abnormalities in protein structure. This hypothesis has received very convincing conformation and has opened up a vast new field of medicine, biochemical genetics.

The exact chemistry of proteins is only just being explored, and it is encouraging to know that much of the work is British. It is fortunate for medicine that the protein chemists have been interested in two proteins of much interest to us, insulin and haemoglobin. The work on haemoglobin is of greatest interest to geneticists. A series of diseases has long been known, characterized by chronic haemolytic anaemia and abnormalities of the red blood cells. These diseases, notably sickle-cell anaemia and thalassaemia, were also noted to be prevalent among certain races and families. The basic disorder in these diseases has been shown to be abnormalities in the haemoglobin molecule. Furthermore it is strongly suspected that the molecular differences are due to changes in the amino-acid sequence of the polypeptide chains. The situation is further complicated because it is known that there are two different polypeptide chains in the haemoglobin molecule, an α chain and a β chain. This probably means that two genes are involved in the 'construction' of a single haemoglobin molecule. The additional evidence needed to confirm this concept is to demonstrate biochemical abnormalities in the genes corresponding to those that occur in the haemoglobin molecule. It is not yet possible to do this. At least twenty variants of human haemoglobin are known. Not all lead to clinical effects. An individual who inherits one abnormal haemoglobin gene will produce both normal and the aberrant haemoglobin. These heterozygotes are said to possess the "trait". It is interesting that there is some evidence that red cells containing sickle-cell haemoglobin (Hb–S) are resistant to malaria parasites. Therefore, individuals with the sickle-cell trait are more likely to survive naturally in malarial zones. This is sometimes cited as evidence that possession of one undesirable recessive gene may, in fact, be of biological advantage. Homozygotes for a haemoglobinopathy are likely to show the full manifestations of the disease with anaemia, splenomegaly and bone changes. Apart from the immense genetic interest of these conditions, they are of some clinical importance in Britain owing to the influx of immigrants of either negro or Mediterranean extraction.

The theory of a biochemical or structural abnormality in a gene altering the molecular structure of a body protein has also influenced the concept of "inborn errors of metabolism". These were familiar to most doctors through the famous Dalmatian coach hound. This animal shares with people suffering from an error of amino-acid metabolism the symptom of alkaptonuria. This is a harmless metabolic quirk. A similar inborn error of protein metabolism is by no means harmless, that is phenylketonuria. Phenyl-ketonuria is a familial disorder characterized by mental deficiency, hyperkinetic behaviour, dry eczematous skin, blonde hair, blue eyes and often epilepsy. Biochemically, there is an elevation of phenylalanine level in the blood and phenylpyruvic acid is found in the urine. The disease is of importance because it is one of the few causes of mental deficiency that are treatable. Treatment, however, to be effective must start early in life. The essential lesion (the inborn error of metabolism) is an inability of the affected individual to convert phenylalanine into tyrosine. This metabolic block is due to inactivity of the enzyme phenylalanine-hydroxylase. It is believed that the enzyme deficiency is determined by the presence of a double "dose" of recessive gene. A single "dose" of recessive gene produce a disturbance of phenylalanine metabolism detectable only by special tests.

If we schematically represent the reaction phenylalanine to tyrosine as, $A \xrightarrow{x} B$. where A is phenylalanine, B tryosine, and x is phenylalanine-hydroxylase, we may represent the phenylketonuric patient as

$$\begin{matrix} A \\ A_1 \not\rightarrow b. \\ A_2 \end{matrix}$$

"A, A_1, A_2," indicate that there is a pile-up of phenylalanine, some fraction of which excess is metabolized abnormally, producing A_1 (phenylpyruvic acid) and A_2 (ortho-hydroxy-phenylacetic acid) which appear in the urine; and "b" indicates a lack of tyrosine and its further metabolites. Although the primary gene effect is exerted on only one enzyme, the clinical effects are widespread. The accumulation of abnormal metabolites leads to excretion of an abnormal urinary constituent, it is probably responsible also for the brain damage and epilepsy. Apart from the effects due to phenylalanine excess there are the sequelae of tyrosine depletion. These include lack of synthesis of melanin and adrenaline, so explaining the lack of of pigmentation and low blood adrenaline.

Phenylketonuria is treated by giving a diet deficient in phenylalanine; this spares the body from excess and the toxic effects therefrom. The diet is expensive, unpalatable, and difficult to control, nevertheless considerable success has been claimed. It is useless if treatment is not started early. Early diagnosis is the best way of getting early treatment and it is obvious that one cannot wait until there are signs of mental retardation. Unfortunately, the disorder cannot be detected at birth. During the early days of life there may be an elevation of plasma phenylalanine, next ortho-hydroxy-phenylacetic acid appears in the urine and only after 3 to 6 weeks does the easily identified phenylpyruvic acid appear. Phenylpyruvic acid is tested for either with (1) ferric chloride or (2) "phenistix" (Ames & Co.).

(1) A few drops of ten per cent ferric chloride solution are added to a specimen of urine, previously acidified with a few drops of HCl. If phenylpyruvic acid is present an intense green colour results.

(2) The end of the test strip is dipped in urine or moistened by pressing against a damp napkin. After 30 seconds the colour change is compared with the colour chart supplied with the strips.

It has been suggested that every infant should have its urine tested for phenylketonuria during the first weeks of life, and in many areas this is being tried. The objections to such a plan are: (*a*) it is difficult in practice to carry out, (*b*) it is expensive—not a serious argument as even with "phenistix" the cost of testing would be about £6,250 per annum for England and Wales, (*c*) the return would not be worth the time and trouble. If universal testing is not advocated it is important that infants at risk should be tested. They are (1) sibs of known cases of phenylketonuria, (2) sibs of mentally defective children who might be phenylketonuric, and (3) all infants who are to be adopted. Finally, screening for phenylketonuria is essential in assessing any mentally retarded child.

It is probable that most inborn errors of metabolism will be found to follow the pathogenetic pattern described. One gene will be found to influence the chemistry and therefore the activity of one important protein. This is as exciting to us as the discovery that all the varied lesions of syphilis were due to a single causative organism must have been to an older generation. From the primary gene effect flow all the secondary effects consequent upon the deficiency of substances beyond the metabolic block, and excess of normal or abnormal metabolites proximal to it. For instance, there is a rare condition of failure to thrive, jaundice, liver cirrhosis, cataract and mental deficiency, a peculiar set of symptoms and signs, which has now been elucidated. Infants with this trouble, which is familial, excrete galactose in the urine. It is known

that the basic lesion is inactivity of the enzyme P-Gal-uridyl-transferase which is necessary for the conversion of galactose to glucose. The apparently unrelated signs of the disease are due either to hypoglycaemia or hypergalactosaemia.

The most common of this rare group of disorders is fibrocystic disease of the pancreas (mucoviscidosis). The primary gene effect is not known, but systems involved include the pancreas (failure of exocrine secretion), the bronchial glands (viscid mucus), and the sweat glands (excess salt). Clinical manifestations vary from neonatal intestinal obstruction (meconium ileus), to intractable pulmonary infection, or steatorrhoea with failure to thrive. It is possible that with the clue of the "one gene, one enzyme or one protein" hypothesis, diseases such as muscular dystrophy may be elucidated. Such diseases cause great anxiety from the genetic viewpoint.

The most common form of muscular dystrophy is the pseudo-hypertrophic type. Unfortunately, its onset is usually in middle childhood so the family may have several children before the condition is revealed. It is usually inherited as a sex-linked recessive, boys being affected and girls transmitting the disease. Of cases at the clinic most have been apparent mutations with a negative family history, but this may be due to selection of cases.

Many problems are posed by genetic diseases of late onset as opposed to conditions apparent at birth. If the parents are aware that a child may be affected with such a disease they will be watchful and anxious for the first signs to appear. This anxiety may affect the medical adviser, on the other hand he may be over-optimistic.

Mr. and Mrs. C. are a healthy couple although Mrs. C. has a history of minor mental disease. Their first child died at the age of 3 years from an acute demyelinating disease (Schilder's disease). They were told that this was an inherited condition. Their second child born after the death of the first showed signs of neurological abnormality quite early. This was somewhat masked because the mother was disabled with puerpural psychosis and the child was cared for by relatives. At 1 year she was not sitting up and appeared retarded. There was much anxiety and the parents could not be convinced the child was not about to suffer from the neurological disease which afflicted their first child. The child is now 3 years and has evidence only of a mild hemiplegia, but agony is hardly too strong a word to describe the feelings of the parents while watching the second child develop.

Mr. and Mrs. M. (S.M.H. 150144)

The third child of this family died at the age of 23 months, following prolonged convulsions apparently starting with an attack of measles. Measles encephalitis was diagnosed as the cause of death. Their fourth child was healthy, as were the first and second. The fifth child died at the ages of 25 months of convulsions diagnosed as hypsarrhythmia. At this time Mrs. M. was pregnant. The sixth child was apparently normal; however, when he was 18 months old Mrs M. was suspicious that he was going the same way as the previous affected children. Neither family doctor nor paediatrician could find definite signs, and Mrs. M. was heavily reassured. At two years the sixth child was dead, having passed through an exactly similar illness.

Mr. and Mrs. P. (30808)

Mr. P. was an apprentice engineer when, at age 18, his shoulders became weak and his facial muscles myopathic. There was a long period of diagnostic argument as to whether his symptoms were due to lead poisoning or to a muscular dystrophy (facio-scapulo-humeral type). When it became clear that he was suffering from muscular dystrophy he had to adjust to a new job and mode of life. This he accomplished, and is now in a responsible clerical post. His son, born in 1942, was watched anxiously and at 16 years showed unmistakable signs of the disease. His adjustment, however, is far less satisfactory and he is bitterly resentful of his inability to play games and to take on any other than clerical work.

It may well be that in certain cases it is inadvisable to enlighten parents concerning the hereditary nature of a disorder as it may provoke, sometimes, needless anxiety; in other cases the anxiety, while justified, may cause maladjustment. Not only the individuals concerned but also the diagnosis and natural history of the disease in question must be considered.

This is an important matter when parents enquire about their children's potential children. Grandparents are often over-anxious and critical, they may be intolerably so if they fear an inherited taint in the grandchildren. One of the most rewarding aspects of genetic counselling is the reassurance that can often be given regarding the children of unaffected members of a family. To reassure justifiably requires considerable knowledge of the interpretation of genetic data.

A group of conditions in which genetic factors are of undoubted importance are the chromosome abnormalities. These seem not to be due to disturbances in the transmission of single genes, but to abnormalities in the chromosome constitution of the gametes during oögenesis or spermatogenesis. Their recognition represents an immensely important scientific advance which has contributed greatly to our knowledge of the aetiology of a relatively common condition, mongolism, and several rare conditions associated with abnormalities of the gonads, Turner's syndrome, Klinefelter's syndrome, and other forms of gonadal agenesis.

Each human cell contains forty-six chromosomes; forty-four autosomes and two sex chromosomes. In the female the sex chromosomes are termed XX and in the male XY. The autosomes are usually numbered. The XX chromosome constitution can be histologically identified owing to the presence of stainable nuclear sex chromatin. This discovery was made by Barr in 1949. Since then, new techniques have made it possible to stain and visualize separately the chromosomes of man (Ford & Hamerton, 1956). Among the earlier rewards of this technique was the demonstration that children with mongolism have forty-five autosomes instead of the normal forty-four. There are now two verified associations with mongolism (*a*) advanced maternal age, and (*b*) trisomy of the chromosomes. It is tempting to relate the two by suggesting that abnormalities of the chromosomes in the gametes are more likely to occur in the "ageing" gonad. There is some evidence that this is so. However, in mongolism there is no conclusive evidence that the chromosomal abnormality is necessarily maternal in origin.

Parents of mongols frequently seek genetic advice. In most cases the mothers are near the menopause and the question of subsequent children is not the important problem. They are more usually seeking an explanation for the misfortune and are worried as to whether their older children may produce mongols. While the new knowledge does not explain the aetiology of mongolism it does enable more information to be given, and the parents can be reassured regarding their children's children. However, some mothers of mongols are young women and it is then more difficult to give a genetic prognosis. Second mongols in a family are very rare but not unknown. It seems reasonable, however, to advise such families not to delay if they are going to have further children, in order to avoid the hazard of advanced maternal age.

It is likely that several more hitherto unexplained conditions may be revealed as due to chromosome abnormalities. So far, the most fruitful area has been in the field of infertility and physical sexual anomalies, multiple congenital malformations, and mongolism. Such cases should receive the benefit of investigation which includes chromosome estimation. The material required is a small piece of skin or bone marrow which is cultured before being prepared for chromosome counting.

GROUP III. DISEASES WHICH ARE FAMILIAL, BUT NO REGULAR PATTERN OF INHERITANCE IS DISCERNABLE

Thirty-three families were seen. Such common entities as asthma, epilepsy, diabetes mellitus, mental subnormality and congenital malformations of the central nervous system form the majority of cases in this large and somewhat difficult group. They may be divided into two main groups; (*a*) the characteristic is modified by the action of several genes and is continuously distributed through the population and (*b*) the genetic influence is heavily modified by environmental factors.

(*a*) Mental defect is a typical characteristic often falling in this group. In most cases of gross mental defect there is a structural or metabolic cause for the cerebral dysfunction. However, in the lesser degrees of defect the brain is structurally and biochemically normal. These people are merely dull, just as many are short in stature or thin in physique. Intelligence (as defined as that quality measured by "intelligence tests") is a largely inherited characteristic. The dull individual born into a dull home is usually well adapted, but consternation however reigns when a dull individual is produced by bright professional parents.

Mrs. B. (60048) had one normal daughter, aged 15, and a mentally defective child of 10 years. The defective child was of normal appearance, had received no brain injury and there was no evidence of a metabolic brain disorder. The family history was studded with dons, writers, and distinguished people in most walks of life. Mr. B. was doing responsible executive work and the possession of a defective child was a severe blow to the parents. Mr. B. was inclined to blame an irresponsible escapade in N. Africa during the war, but one of the distinguished consultants that had seen the child said "it is undoubtedly hereditary and will almost certainly crop up again in the family". If this was meant to console Mr. B. for his night of venery in Alexandria it did so at great cost, for it not only placed a stigma on the family past but filled Mr. and Mrs. B. with fears for the future. In this sort of case we do not know the answer and *primum non nocere* must be the main part of any advice given.

(*b*) Genetic influence modified by environment. In this group come a great many interesting conditions, asthma, some cases of epilepsy, diabetes mellitus, coronary thrombosis, obesity, susceptibility to cancer and tuberculosis and, no doubt, many others. The diseases are undoubtedly familial, but do not follow a regular Mendelian pattern of transmission. Genetic prognosis must be given largely on statistical grounds. Roberts (1959b) has emphasised that from the counselling aspect the more obscure the genetic element the better in general is the genetic prognosis. The application of this principle may be justifiable in reassuring parents but should not lead to the application of less energy in determining the true place of inheritance in these diseases. In order to get the statistical information required large numbers of cases must be studied together with family trees. In some of these conditions advice is sought largely for the sake of the mother, in others for eugenic reasons.

(i) Lethal congenital malformations. About twenty per cent of still births and neonatal deaths are due to congenital malformations. Of these, eighty per cent affect the central nervous system (anencephaly, spina bifida cystica). It is commonly believed that there is a genetic influence in the aetiology of the malformations, as they are more likely to be repeated in a family than can be accounted for by chance. Proof of this is lacking but much more information is required than is currently available about the incidence of these prevalent and distressing conditions. The recurrence rate is low and even after a mother has had two such malformed infants the probability of future normal children is quite good. Family limitation if practised is largely to spare the mother the stress of unsuccessful pregnancy. Genetic advice is limited to giving the statistical chances of recurrence and to stressing the hopeful outlook that is justified.

(ii) Eugenic reasons. Conscientious parents knowing of a condition such as asthma, epilepsy or diabetes in the family may feel that they should not have children if they are likely to be sufferers from these conditions or propagate them. Sometimes the motives behind a consultation are less altruistic.

Mr. and Mrs. H. (58896)

Mrs. H. is a young 19-year-old who has suffered for petit mal since the age of 5. She is not seriously handicapped although still on medication. Her parents disapproved of her choice of husband and as part of a campaign of persecution, they said she should not have children because "they were bound to be epileptic" and also suggested that Mrs. H. would not be able to look after them.

It is impossible to give an accurate genetic prognosis in such a case; Mrs. H.'s epilepsy may well be due to birth injury or some other environmental factor, but if genetic the chances of her children being affected are probably small (approximately one in forty), and there are many people prone to epilepsy who have no or few fits. In this case there is, however, the problem of Mrs. H's own fits. The geneticist is not however, concerned with predicting whether a mother will be physically or mentally fit to look after her child. That is another facet of the total problem.

Whether those not physically fit should reproduce is a difficult question, and one which the geneticist would not care to answer in an individual case. Undoubtedly as the treatment of diseases such as diabetes mellitus, haemophilia, asthma and epilepsy improves, more sufferers from these conditions will be able to live normal lives which include reproduction. None can say that an increase in people suffering from these diseases will seriously weaken the human race. They may have qualities which distinguish them from the ordinary in a beneficial sense and thus contribute to rather than detract from the community's welfare. These conclusions apply in some measure to the problems of consaguinity in marriage and to A.I.D.

Miss R. and Mr. M. (56532) were proposing to marry. They are first cousins and the family history disclosed: (*a*) menopausal psychosis, (*b*) "mild" form of epilepsy, (*c*) Paget's disease of bone, and (*d*) mental defect.

None of these conditions is known to be due to recessive genes and there was no reason to interdict the marriage. Degrees of consanguinity other than incest and first cousin matings are probably quite unimportant. Incestuous matings are likely to manifest undesirable recessive characteristics. First cousin marriage increases the relative risk from recessive genes, but the actual risk is not considerable. There is some evidence that the offspring of first cousin marriages tend to be infertile. Problems of A.I.D. have not as yet appeared at the genetic clinic. The major genetic hazard of A.I.D. would seem to be a remote possibility of a person marrying his or her half-sibling. Such an occurrence would be extremely rare and not necessarily harmful. Obviously, a donor of spermatozoa should be chosen who is free from obvious inherited disease, and in this respect the child born by A.I.D. may have a superior genetic endowment from his "selected" father than from one chosen by chance!

In our experience genetic advice is welcomed and usually we find that the genetic prognosis is better than the patients had thought possible. It is likely that many parents would appreciate genetic advice but do not like to ask, or do not realise that it is available. The accuracy and value of such advice has been greatly increased by the new facts of genetics, and human genetics has a considerable part to play in the advancement of scientific knowledge.

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REFERENCES

Barr, M. L., Bertram, E. G. (1949). *Nature* (Lond.) **163,** 676.
Ford, C. E., Hamerton, J. L. (1956). Ibid, **183,** 302.
Hsia, D. Y. (1959). *The Inborn Errors of Metabolism.* The Year Book Publishers Inc. Chicago.
Nance, W. E. (1959). *Medicine* (Baltimore). **38,** 403.
Roberts, J. A. F. (1959a). *Brit. Med. Bull.* **15,** 129; (1959b). *An Introduction to Medical Genetics.* 2nd. edition. Oxford University Press. London.

PAIN*

BY

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Pain is perhaps the commonest symptom for which our help is required. Its interpretation, assessment, and alleviation is the main problem facing the doctor. The word is used for two separate, if often related, phenomena. The first is the unpleasant sensory experience that results from bodily injury or disease. The second is an emotional disturbance which usually accompanies and colours the sensory experience of pain, but which may on occasion result from purely psychological disorders.

THE ANATOMY AND PHYSIOLOGY OF PAIN

(*a*) *Pain pathways.* Pain fibres from the trunk and limbs enter the spinal cord in the posterior root, ascend on the same side, usually for about three segments, and end in the posterior horn cells of the same side. The next relay crosses immediately to the lateral spinothalamic tract of the opposite side and ascends in this tract through the cord and medulla to the pons, where it joins the lateral portion of the median fillet, passing upwards to the ventral nucleus of the thalamus. The next relay passes through the posterior limb of the internal capsule and the corona radiata to end in the post-central region of the cortex. Pain fibres from the face enter the pons through the Vth cranial nerve and turn downwards in the descending tract of the trigeminal nerve to end in the nucleus of this tract, which descends as far as the second cervical segment of the cord. The next relay crosses in the medulla and ascends in the quinto-thalamic tract to join the spinothalamic tract, and so reaches the ventral thalamic nucleus.

(*b*) *Cortical projection of pain.* Impulses travel from the ventral nucleus of the thalamus to the cortex. From experiments on monkeys, it seems that a definite topical plan exists, whereby fibres from the inner portion of the nucleus end in the lower part of the gyrus, those from the outer portion in the paracentral region, and those from the middle portion in the intermediate part of the post-central convolution. This does not, however, tell us how pain is appreciated. It is only possible to gain insight into this by assigning functions to structures in the light of the defects produced when a portion of the pain system is destroyed. Appreciation of pain arises from structures at or above the mesencephalon; a lesion of the upper pons will abolish peripheral pain. Small lesions of the cortex produce little or no impariment of appreciation of pain. Larger lesions, however, will at times produce hypalgesia of mild or severe degree. More frequently they produce an inability to distinguish between pains of different qualities. In a case of hemispherectomy cutaneous sensation was lost everywhere except in the face; joint sense was not affected. It must, therefore, be concluded that extensive cortical lesions may produce varying degrees of hypalgesia, with the face much less affected than the rest of the body.

(*c*) *The mechanism of common sensibility.* Weddell and his colleagues have recently drawn attention to the impossibility of equating the four commonly recognized modalities of cutaneous sensation—touch, warmth, cold, and pain—with four separate and distinct kinds of nerve endings in the skin. To determine whether a particular nerve

*Based on an address to the Bristol Medico—Chirurgical Society.

terminal is related to a particular sensation such as pain may appear a straightforward question, but it is not. There are two theories. The commonly held view is that pain is subserved by a specific set of pheriperal sensory nerves and their specific nerve-endings. More recent work has cast doubt on the presence, certainly in hairy skin which covers the greater part of the body, of circumscribed nerve endings such as Meissner's corpuscles, Krause end-bulbs, and so on. Instead, there are widespread arborisations of fine, freely-ending filaments which interweave, the so-called free nerve endings. Lele's work suggests that sensation of heat is in some way connected with the pattern of the discharge evoked from the skin, and not just to the discharge from specific nerve endings. It has also been shown that the mode of innervation of hair on the rabbit's ear is multiple and complex, each hair being served by at least two dorsal root axons. The average is about six, and there may be as many as twenty involved. It has been calculated that every root axon could be made to discharge simultaneously if no more than one quarter of the total hairs on the area were stimulated. This can only mean that hair messages are coded for transmission, and reach the central nervous system as sets of spatially and temporally dispersed action potentials which are then presumably decoded. There can be no question of each hair having a private and exclusive line.

Weddell brings further evidence and argument to suggest that free nerve-endings and the nerves subserving them in the skin are arranged in a similar way. His work has shown that all the modalities of senation are independent of their so-called specific nerve-endings, Meissner corpuscles and the like, and suggests that pain, for example, is a mathematical summation of the temporal and spatial distribution of impulses passing centrally along peripheral nerves.

(*d*) *The pain of inflammation.* There are probably various factors concerned, which include increased tension from rapid distension of soft tissues, increased accumulation of metabolites (the raised local temperature favouring their production), and occlusion of the circulation which may act by hindering the removal of metabolites or by producing anoxia of the tissue.

Keele's work with fluid drawn from blisters, pleural effusions, or rheumatoid joints, which causes pain when applied to a raw surface, suggests that tissue damage brings about the release of an active proteolytic enzyme, which in turn acts upon the plasma to form pain-producing substance (P.P.S.). Thus in addition to the effects of tension, metabolites, and ischaemia, pain in inflammation may be caused by the release of 5-hydroxy-tryptamine, histamine, and P.P.S.

(*e*) *Vascular causes.* It is not disputed that ischaemic pain is due to anoxia, whether that be relative, in the presence of excessive muscular activity (intermittent claudication), or absolute from vascular spasm (angina pectoris). It is not yet established whether oxygen deficiency either leads to the accumulation of metabolites or interference with their removal. In reference to visceral pain, it is of interest that William Harvey performed several experiments on the son of Count Montgomery, a friend of Charles I. The child had suffered a severe accident, which left him with his heart exposed, and its beating could be easily seen and felt. Touching the heart produced no sensation. It was therefore assumed that what had been regarded since Aristotle as the "seat of the soul" was insensitive. What then was the cause of cardiac pain? We now know that it is ischaemia.

(*f*) *Multiple causes.* The pain of hiatus hernia is usually felt below the sternum and may radiate to the back. Sometimes, however, it occurs higher up and is identical with angina; in which case it has been noted that successful repair of the hernia appears to cure the pain, though it may recur in the same form several years later. There is experimental evidence for the view that this pain originates in the heart, and is induced by a disordered oesophagus. The introduction of an inflated balloon into the lower end of the oesophagus of healthy young anaesthetised dogs causes a reduction of coron-

ary flow of up to 50 per cent. It is thus clear that if the coronary flow is already reduced by atheromatous changes, further reflex reduction would be likely to cause angina. The fact that hiatus hernia in young persons never causes typical anginal pain with radiation to the arm would seem to support this. A similar association of anginal pain with gall-bladder disease exists clinically. Again, experimental mechanical stimulation of the bile ducts outside the liver has been shown to reduce coronary flow by at least 50 per cent. Improvement in the angina which follows removal of a diseased gall-bladder is often dramatic. In the same way, therefore, gall-bladder disease is more likely to cause angina when there is a pre-existing reduction in coronary flow from atheroma.

CLINICAL ASPECTS OF PAIN

In these days of high-powered diagnostic instruments the importance of a careful analysis of a history of pain is insufficiently stressed; the process of unravelling an often confused description is all too time-consuming to be popular in a busy out-patient clinic; but it is invaluable when pain is the sole complaint. The experienced clinician automatically analyses the quality of pain by following a definite thought-plan: "Pain—new or chronic? Patient—healthy or ill?" He observes and subconsciously records the walk of the arthritic, the bland expansiveness of the unoccupied widow, the sweat on the brow of the anginal traveller, the paunch of the diabetic with neuropathy, the hang-dog, truculent attitude of the compensation-seeker. He has taken all this into account before he considers the details of site, distribution, type, and depth of pain. He remembers that each man's conception of pain is made up of his own personal experience, together with such accounts of their pain as other people can give him. As Kellgren points out, even the trained investigator acting as his own guinea-pig finds it difficult to translate sensory experience into words. How much more difficult for the average out-patient, especially when the emotional component is high! And the appreciation of pain cannot be separated from the emotional make-up of the individual. Stick a pin into one man and he says stolidly "It's a prick"; another will scream and withdraw violently. The indifference of the leucotomised patient to fully-perceived pain can in a homely way be exemplified by comparing one's own reaction to a painful injury after a champagne and brandy-lightened dinner with that to a similar injury after a cup of hot black coffee on a cold winter morning.

Pain in children

In the neonatal period, we believe there is a relative indifference to pain. The baby can be circumcised without an anaesthetic, provided it is happily sucking a bottle. Later on, after a month or two of life, pain is felt, but imperfectly localized. Thus pains from abdominal colic, otitis media, or bone inflammation may all produce the same reaction—screaming, drawing up of the legs, vomiting and convulsions. The drawing up of the legs may be translated by the mother as "the wind"; beware of accepting her diagnosis!

Gradually, through childhood, localization becomes more distinct, though still imperfect, especially in respect of the abdomen. At this age inability to localize pain in the head is not a sign that it is psychogenic. Suspect, rather, the child who complains of "dreadful pain". Again, a child with a sore throat rarely complains of it; he goes off his food and may vomit. This is not necessarily a disadvantage; you will remember the great Dr. S. J. Gee's advice to young doctors—"Eyes first and much, ears second and little, hands not at all". In early infancy, then, do not expect pain or its accompaniments. Later on, do not expect accurate localization. Let your examination be thorough.

In appendicitis in childhood pain is always present, but the difficulty is that so many other conditions may cause pain in the belly. If our examination is cursory, and if we

are not prepared constantly to be on the watch for this possibility, the child may slip away; and the younger the patient the more rapid is that process. Pericarditis is now a rarity in childhood, but no one having seen it will forget the desperately ill, toxic child whose illness throughout has been unaccompanied by complaints of pain.

The general reaction of children to pain is good. Like dogs, they tend to crawl away and get better. This tendency, of course, is modified by the mother's reaction to the situation, and by the association in their minds of doctors and pains, and often by fear of what the doctor may do. How often we are greeted by "You are not going to look at my throat, are you?"

Apley has pointed out that there are suggestive links between the usual, recurrent, non-organic pains of childhood, whether they occur in the limbs, abdomen, or head (the only common sites in this age group). In studies carried out over a number of years interesting similarities were observed, not only between children who made similar complaints, but also between their families. He suggests that those pains may be grouped together as expressions of a reaction-pattern, which is usually associated with emotional disturbances both in the child and in other members or the family.

Pain in the aged

On the whole the aged show less outward expression of pain, less tendency to be restless or to cry aloud, unless they be demented when the pain threshold is raised. Some of the pains they suffer are devastating—the particular hell of post-herpetic neuralgia; another hell for *tic douloureux;* and a third for ischaemic pains in the limbs with "the jumps". But perhaps the "horizon pain" is worst of all—the bleak, long, comfortless night across the ocean of sunless misery.

On the other hand, the old ones tend to complain less of their peptic ulcers, and hardly at all of toothache even in the presence of hideously infected teeth. Again, the older the patient the more likely it is that circumstances will permit him to rest the part; in fact pain may be a cause of immobility in old age.

In addition to post-herpetic neuralgia and *tic douloureux*, it is well to be on the lookout for giant-celled arteritis (including temporal and cranial arteritis, which may of course present typically with temporal or occipital headache) which may begin insidiously with pyrexia, malaise, and "fibrositic" pain in head, neck, or shoulders. It is important to recognize this disorder because of the danger of sudden blindness. Osteoarthritis of the hip is another geriatric pain problem; if pain is present at rest or in the night, radiotherapy will sometimes help.

The Rheumatic Group

Pain is *the* dominant complaint of all rheumatic sufferers. In some form or other it is constantly forcing itself to the surface of any activity, and when it abates its room is as conspicuous as its presence. It may for long be the only symptom, recurring for varying periods without any other evidence of disease, and without being in itself dangerous or seeming to provide a protective mechanism. Its interpretation, assessment, and alleviation is the main problem facing the doctor.

(*a*) *Neuralgia.* So-called characteristic features include the paroxysmal nature of the pain, absence of clinical signs, and absence of pathological findings. None of these stands up to critical assessment. *Trigeminal neuralgia*, the prototype, the neuralgia *par excellence*, pure pain, has already been alluded to. Those who favour a strict differentiation between neuritis as an organic disease and neuralgia as a functional disease draw their main support from this. How does it fit into the criteria mentioned above? Not at all. It is not always paroxysmal in the mild cases; minor sensory changes may be present in the direction of reduction in sensation; modern methods of staining do show changes in the cells of the Gasserian ganglion; trigger zones are not always present; and it may be associated with herpes simplex. The existence of a *true occipital*

neuralgia is also doubtful, for the pain is either a neuritis from root pressure in cervical spondylitis or a myalgia of vascular origin. In both cases rest, warmth, and a firm pad in the nape of the neck at night are more rewarding in my experience than resort to the physiotherapy department or the chiropractor. A simple rubber collar is effective for the same reason. Remember that manipulation of the neck can precipitate vertebral thrombosis.

(*b*) *Acroparaesthesia and the carpal tunnel syndrome.* One of the commonest types of patient seen in the rheumatic (and, I suspect, the neurological) clinic is a tired worn-looking woman of 40–60 years, who wakes up in the night with painful paraesthesiae in the fingers, and pain in the forearm, sometimes extending as high as the shoulder. The fingers feel stiff and swollen, and are clumsy. There are normally no physical signs, except very occasionally impaired sensation over the tip of one or two digits. The term "acroparaesthesia" was introduced by Schultze in 1893 to describe these largely nocturnal symptoms in women. In 1945 Walshe put the problem on a sounder basis, suggesting a mechanical cause—traction or compression of the brachial plexus or the subclavian artery, or both, between the clavicle and the first rib, as a result of sagging of the shoulders from fatigue. Obliteration of the radial pulse by dragging down the arm is usually easily obtained. Middle-aged women, often of the middle class, are the chief sufferers. Is it because they have to tackle housework to which they are not accustomed and cordially dislike?

A special variety is seen in the last trimester of pregnancy, usually after the 32nd week; it clears up within hours of delivery, and can be relieved earlier by promoting water loss. Some of these women relapse later on, probably for two reasons—increase in weight, and the extra activity required in looking after the baby. The essential principle of treatment is always a preliminary period of rest in bed. Later, when rested, help may be obtained from heat (to promote muscle relaxation), light massage, and bracing exercises for the neck and shoulders. In the early stages all forms of physiotherapy aggravate the pain.

The recognition of the carpal tunnel syndrome as a cause for some of these symptoms constitutes a great advance in the elucidation of pain in the upper limb, and has to some extent shifted the onus from the costo-clavicular space.

My own view is that sensory or motor disturbances resulting from pressure in the costo-clavicular space are precise in pattern, corresponding to the distribution of the 1st dorsal nerve. In severe cases there may be a certain amount of over-spill, but the symptoms are rarely vague or widespread. When the pain is described as affecting the arm and the forearm, perhaps spreading into the neck or the side of the chest, without muscle wasting, suspect spondylitis, with or without postural faults. When the area affected is confined to the forearm, and especially to the outer border of the hand, suspect pressure on the medium nerve in the carpal tunnel. In the latter case, a careful examination will reveal slight wasting on the outer side of the thenar eminence with loss of sensation on the palmar aspect of the index and middle fingers. Unfortunately, cervical spondylosis and sagging of the shoulders are extremely common in women of this age, and it is not long before a psychogenic factor becomes superimposed.

(*c*) *Backache.* Space does not permit a proper consideration of shoulder-girdle pain or of sciatica, but I must spare a few lines to marshal some arguments against the absolute supremacy of the inter-vertebral disc in the doctrine of backache and sciatica.

(i) Protusion of the intervertebral disc in the lumbar region is very common in later life and is a frequent autopsy finding, without any history of pain. We may have pain without a "disc", and a "disc" without pain.

(ii) The evidence is against the importance of trauma. Patients in general, not excepting those with sciatica, have an overwhelming desire to attribute their

troubles to external factors, particularly trauma. Often, on close questioning, the pain is found to have occurred before the accident.

(iii) In many cases at operation (26 out of 100 in Wartenberg's series), no disc protrusion has been found; and it is well to remember that in simple neuritis laminectomy helps by virtue of its decompressive effect.

(iv) Some patients complain that their sciatica followed exposure to cold.

(v) Sciatica occurs with herpes zoster, or following acute infective states such as brucellosis or tonsillitis.

(vi) Neuro- and orthopaedic surgeons tend to base their views on severe and intractable cases which have resisted all other forms of treatment. They do not see the mild cases, which may be transient. Three out of four cases recover quickly with medical treatment (warmth, rest, analgesics, and a firm bed). It is unlikely that these remissions depend upon the retraction of a prolapsed disc. Sciatica is, in my experience, a benign affair, and clears up within two or three weeks. It is to be fervently hoped that this unfortunate intermezzo of disc hysteria will now abate. As the French say "On affaiblit toujours tout ce qu'on exagère". Two other quotations spring to mind: "We were better off with lumbago and sciatica when we knew nothing about discs" (Brailsford); and "Surgery of the intervertebral disc is major surgery, and the penalty of error is severe" (W. T. Mixter).

(*d*) *Panniculitis*, or "tension syndrome" is thought to be due to distension with fluid of the fatty tissues where they lie within an indistensible fibrous covering. The main factor is vascular, but there are probably endocrine influences. The patient is often obese, and the areas affected include the outer parts of the shoulders and thighs and the internal fat pads of the knees. The syndrome, if it occurs before the menopause, is generally most painful in the pre-menstrual periods. A characteristic sign is the peculiar *peau d'orange* effect when the thickened skin in the painful area is picked up. The prognosis is good if adequate treatment is given early and persevered with; this includes a reducing diet, salt restriction, exercises, hydrotherapy, and massage.

(*e*) *Fibrositic pain.* I should like to suggest that after the separation of such definable entities as tendinitis, bursitis, panniculitis, fat herniation, and psychogenic rheumatism, there remains a group of individuals with a diffuse or localised soft tissue pain and stiffness in whom, in the absence of clinical, laboratory and X-ray abnormalities, the diagnosis of "fibrositis" seems justifiable. The earlier concept of local inflammatory change in muscle and connective tissue is now quite discredited, and should be discarded. I should like to suggest boldly that the fundamental factor is vascular, and that the pain in muscles and soft tissues is ischaemic pain. Interference with blood supply may result from spasm or from atheromatous change in the arterioles, or from a combination of the two. It is a matter of observation that many chronic rheumatic patients are elderly and suffer from other results of circulatory disturbance. Equally, many show the stigmata of tension, anxiety or depression. Vascular spasm is probably reflex, and can be brought about by a wide variety of stimuli, which include postural faults, muscle over-fatigue, temperature and humidity variations, nerve root pressures, and (commonest of all) psychogenic influences. Elliot, in 1952, showed by electromyography that the tender areas found in muscles are due to localized spasm. The tender spots, or so-called "fibrositic nodules" are usually, but not always, of this type. Nevertheless, the diagnosis of fibrositis is beset with pitfalls. Here are a few: *With fever*, think of rheumatic fever (the forgotten disease), subacute bacterial endocarditis (the missed disease), brucellosis and glandular fever (the over-diagnosed diseases). *With wasting*, think of cancer and any of the collagen disorders (the fashionable diseases), temporal arteritis and hypernephroma (the undiagnosed disease). *With anaemia*, think of these and of chronic renal failure. Do not forget the pains of metabolic bone disease.

The connection between steatorrhoea and osteomalacia is well known, but the steatorrhoea may for long be occult and the patient may complain only of generalised fibrositis-like aches and pains, with tenderness of the bones and a waddling gait.

Psychogenic Pain

Is the pain real? To the patient all pain is real, except for the true malingerer. If we identify the word "real" with adequate organic cause, then there are pains which are definitely not real. And here I would remind you that it is indefensible to call any pain or any symptom "neurotic" simply because you cannot immediately find an organic explanation, or, which is even more pertinent, because there are surrounding circumstances tending to neurosis. There must be both absence of organic signs and the presence of other stigmata of anxiety or hysteria. Psychogenic causes, in my experience, predominate in the non-articular group of rheumatic diseases, properly designated "rheumatics". How shall we hope to recognize psychogenic pain? The patient projects his unhappiness into some part of the body where he keeps it quite cheerfully as an "agonizing pain". These pains are often bizarre in distribution and described with drama snd detail. The more ubiquitous the pain, the more is it likely to be neurotic. Conversely, when a patient month in and month out points to one place you can be reasonably certain there is an organic cause. There are the people (the anxiety neurotics) in whom mental tension expresses itself in widespread muscle spasm —they move awkwardly and stiffly, contracting agonists and antagonists simultaneously; this leads to fatigue and painful muscle strain. In hysteria, which is rare, the pain is used to achieve a particular personal aim, usually that of escaping from a difficult situation or fulfilling a desire. In studying the patient, other psychogenic disturbances or obvious constitutional inadequacy will appear. Then, there is usually a history of multiple consultations, innumerable investigations, months of physiotherapy and repeated operations—and, in spite of this, or because of it, the patient will often complain of the unsuccessful treatment carried out by former doctors, and of their negligence and ignorance. Remember that your turn, too, will come. You will be lucky if you do not end up by introducing yet another iatrogenic symptom. We must also remember that pain may become an "old friend", and there are occasions when we do the patient a disservice by attempting to undo his solution of an agonizing problem.

We must not be afraid to tell the patient, after a careful examination, our findings and conclusions. I have been astonished to note how often, if the explanation is given quietly and in a kindly, sympathetic manner, the psychogenic patient is willing to accept it, and this understanding of the problem of tension and spasm as a cause for pain is more than half the battle. Beware of the alternative line of sending such patients to swell the ranks of chronics littering the physiotherapy departments all over the country. In these departments it has long been recognized that spastic areas in muscles are the site of pain and that such pain can often be temporarily relieved by the application of heat and massage, or by the injection of a local anaesthetic; but only temporarily, for it requires much more than this to get to the root cause and break the vicious circle. This is not to suggest that physiotherapy has no part to play in the management of the psychogenic rheumatic; provided that the patient fully appreciates that it is only part of the plan of treatment and provided also that the importance of achieving relaxation is fully understood, it can be useful.

Pain—Friend or Foe?

I should like now to strike a philosophical note and introduce a conception of pain as a physiological function in a pathological environment. That pain, long continued, wears the sufferer down, none can deny. Yet pain alone could be harmless. It is the secondary effects that do the harm—shock from sudden pain, inactivity, depression, and fear of prolonged pain. Of all pains, none is more terrible than that of invasive

cancer. By contrast, consider the pain of trigeminal neuralgia. Whereas the one keeps up its relentless barrage right up to the moment of death, the other, exquisite agony though it may be, will suddenly lift, and the victim, seconds earlier driven almost out of his wits, becomes at once his normal self. May I be privileged to remind you of the contribution of a distinguished West Country man, himself both physician and philosopher, to the literature of pain. John Locke was born in 1632 at Wrington, at the foot of the Mendips. His vivid description of a paroxysm of trigeminal pain in the Countess of Northumberland, wife of Charles's trusted ambassador in Paris, is a veritable masterpiece, and I cannot imagine that it has ever been equalled for its objective and scientific clarity, both relieved and emphasized by the warmth of Locke's understanding. In describing the incident to his friend, Dr. Mapletoft, he was giving the first account in Europe of *tic douloureux*. Here, surely, is pure pain, unalloyed by the consequence of organic disease. It has the simplicity of physical signs in children, uncomplicated as they are by the legacies of earlier pathology.

I believe that Philip Hench's most important contribution to rheumatology was his concept of the reversibility of rheumatoid arthritis (as exemplified in jaundice and pregnancy). I suggest that this concept be extended to pain and that we think of its reversibility and, in a sense, its essential benignity. This latter is not a quality usually attributed to pain, but it might be granted to a function that is strictly physiological. Where there is pain, there is also life. Death and the grave are painless. We see a charade of this in rheumatism; when the process of destruction has gone beyond a certain point pain disappears, as in advanced stages of arthritis mutilans. So long as the injured tissues can respond physiologically to disease by giving rise to pain, then reversibility and recovery are still possible. Pain is a sign of life. A similar analogy comes to mind when we contrast dental pain and its subsidence with death of the tooth.

We can sometimes envisage pain as a local protective mechanism, interference with which may encourage a damaging level of performance and bring about permanent destructive changes. As examples of this, I well remember two patients with recurrent effort angina in whom pain, continuing in spite of all the usual measures, was finally controlled by stellate ganglion block. Within a short time both patients were in serious heart failure, probably as a result of the extra exertion hitherto prevented by the pain. Steroids in the treatment of rheumatoid arthritis, by relieving pain and spasm, often permit a level of activity for which the joints are not prepared or the muscle tone adequate, with the result that destruction proceeds apace. Recently, Evans and his colleagues have drawn attention to the danger of intra-articular hydrocortisone which, by its anti-phlogistic and analgesic effect—often quite spectacular—permits a damaging level of activity so that destructive changes occur, which, if not obvious clinically, are only too obvious in serial X-rays.

TREATMENT

(*a*) *Analgesics.* I agree with McIlwain that "opium has probably contributed more than any other preparation to faith in the healing art and belief in the feasibility of lessening human ills by administered drugs". Knowledge of analgesic drugs has been limited by lack of any reliable method of assessing their effects. Recent work by Wolff, Hardy, and Goodell has greatly added to our knowledge, They devised methods of quantitively assessing the action of analgesics and analysing the various factors that modify their effectiveness. All the commonly used analgesics (morphine, codeine, alcohol, aspirin) were found to raise the pain threshold in that order of effectiveness, and for each there was a dose producing a maximum or ceiling effect, which was not exceeded by further increasing the dosage. In the course of their studies, they became aware of other valuable effects, beyond the mere heightening of pain threshold, effects particularly upon the mental state of the individual. It seems clear that, in the absence of anxiety regarding its source, pain is comparatively well tolerated.

The effect of the mental state upon the pain threshold is well recognized by drug manufacturers and, of course, is the main reason for the relative effectiveness of morphia. Pain threshold can be raised by as much as 30 per cent by suggestion through placebos. Greater rises, but lasting for a shorter time, have been obtained by distraction.

These considerations call for a change of emphasis in regard to the mechanism of action of pain-killing drugs, and may perhaps explain in some way the popularity of various faith-healing cults. Analgesic drugs are useful in the treatment of pain, but their full effect can only be achieved when the physician commands the full confidence of his patient.

(*b*) *Surgery*. Intractable visceral pain is often due to the direct extension of the morbid process into the spinal nerves. In such cases, section of the posterior spinal nerve roots (posterior rhizotomy) may be a valuable procedure, provided that the area affected is limited to a small number of spinal segments. When a large number of spinal roots are involved cordotomy may rarely be justifiable. Posterior rhizotomy is a serious and hazardous operation. It has its greatest use in the treatment of severe localized pain in the neck and trunk, for example in bronchogenic carcinoma beginning in the apex of the lung, carcinoma of the breast invading the chest wall, and intractable angina.

Surgical relief of *tic douloureux* should, if possible, be conservative. Section of the sensory root behind the ganglion under the best of conditions leaves an uncomfortable, stiff, swollen feeling in the face and tongue. 5 per cent may get facial paralysis; 5 per cent a persistent burning sensation in the anaesthetic area. The patient's gratitude to the surgeon does not last. A better method is the use of alcohol injections into the appropriate branch of the trigeminal nerve.

In the past leucotomy has been advised for pain only when all other possible methods of treatment have failed. This as, McKissoch has said, is bad practice, and few will disagree with his view that what in a final analysis proves the most beneficial operation should be the initial one. Elithorn, Glithero, and Slater have carefully studied the results of this operation in twenty-five patients with intractable pain followed up for from two to six years. They confirm the previously held view that leucotomy does not affect the perception of pain and their findings suggest that the immediate autonomic and behaviour disturbances aroused by a new painful stimulus are, if anything, greater after leucotomy damage. On the other hand, such disturbances are less prolonged and less readily aroused by fear of a repetition of the pain. It must be remembered that leucotomy, while causing a shock effect similar to that produced by electroconvulsive therapy, with the breaking up of established moods particularly of depressive type, also produce a focal and persisting neurological deficit resulting in changes in the disposition of the patient, in particular a reduction in the tendency to become anxious. Typically, in such cases the patient still complains of pain, but shows at the same time an inappropriate cheerfulness. Ordinarily, this would suggest hysteria, and, in fact, in Elithorn's series, those patients showing hysterical features before operation became more hysterical afterwards.

In selecting cases for this operation, the main indication is pain in association with an excessive psychological reaction in the anxious, introspective, depressive type. The more definite the physical pain, then the less likely is it that leucotomy will help. Since the risk of either excessive personality-change, post-operative epilepsy, or operative death amount to about 10 per cent, it is clear that damaging operations on the frontal lobes provide no satisfactory answer and are only justified if a direct attack upon the pain is impossible.

THE EVOLUTION OF PAEDIATRICS*

BY

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The City of Bath has known many famous men. Today I pay tribute to the Reverend Thomas Robert Malthus. He first came to Bath as a schoolboy, though he learnt little but Latin and good behaviour from his teacher, the Rector of Claverton. When he returned many years later (in 1834), to visit his wife's family, Malthus had achieved lasting fame. He died suddenly of heart disease, and was buried in Bath Abbey. An inscription to him can be seen just inside the door on the left of that gracious honey-coloured building. It describes his integrity, sweetness of temper, benevolence and piety; yet paradoxically, because of his views on the limitation of populations, he was "the best abused man of his age".

Malthus played a vital part in Darwin's theory of evolution. He described the trend of populations to increase faster than their food supply. When Darwin read Malthus's work it gave him the essential clue to natural selection: if species produce too many offspring to survive, the weakest will die and the strongest live. And, to come to my subject, because this year is the centenary of Darwin's *The Origin of Species* I have been stimulated to consider paediatrics from the evolutionary aspect.

Before I go on to discuss paediatrics in terms of evolution let me first briefly continue the Malthusian theme into our own day. It is estimated that in Biblical times the population of the whole world was about the same as is that of the United Kingdom now. Last year the world population *increased* by approximately the same number. The rate of increase is accelerating, but in the world as a whole the production of food is not keeping pace.

Can this Malthusian dilemma be solved? It might eventually be solved by "fertility control", as it has been called. There are already oral methods of contraception for women; and the sterilization of men by vasectomy is practised in at least one overpopulated country in the East. From the opposite approach, the production of food may increase startlingly, by photosynthesis, for example, or by the harvesting of the oceans. Will these methods solve the problem, or merely postpone its solution?

An eminent scientist recently suggested that the population problem is likely to be solved catastrophically. He and others—may I dub them Malthusiasts?—forecast that a population "crash" is imminent. One of three outcomes is anticipated. A trigger-happy politician with a large store of nuclear weapons may abolish at the same time our worries about population and most of the population itself. Or a virulent infective agent may appear, like myxomatosis in rabbits. Or we may be overwhelmed by a "stress syndrome", like that which affects voles and jack-rabbits in periods of overpopulation.

To us as doctors possibly the most immediately relevant aspect of Darwin's theory is the law of adaptation. Species or sub-species adapt themselves to their environment: they adapt or perish. I am going to apply this tentatively to paediatrics, which may be considered one of the latest sub-species of medicine; for a sub-species is a section of a species that has become sufficiently differentiated to deserve a name of its own, but can still inter-breed with the rest of the species. In retrospect, the course of

* An address to the Bath Clinical Society on 13th November, 1959.

change in successful evolution appears to be not haphazard but directional; there is progress, usually from simple to complex and from lesser to greater efficiency. This certainly applies to paediatrics. Again, the evolution of vertebrates goes with a continuous exploration of new environments: paediatricians with a backbone are continually exploring new environments.

THE EVOLUTION OF PAEDIATRICS

Such speculation stems from Malthus, whose work gave Darwin the idea on which the theory of evolution was based. But even evolution is evolving, and since Darwin's time we have come to realize that natural selection is increasingly being modified by human selection. Julian Huxley has pointed out that we have reached a critical phase in the development of our planet: the evolutionary process, as now embodied in man, has for the first time become aware of itself. "Evolution", Huxley wrote, "is on the verge of becoming internalized, conscious and self-directing". As I see it, the value of discussing paediatrics, or any aspect of human affairs, in terms of evolution is that we may learn from the past and become self-directing.

Primitive civilizations practised infanticide, cannibalism and ritual sacrifice. Twins were regarded as unnatural, and done away with; so were babies born with teeth, those who sneezed directly after birth, and those born on unlucky days or in stormy weather. A sense of responsibility to infants and children has developed remarkably through the centuries. We accept now that the attitude of the tribe or nation towards its children is a barometer of progress; dare I suggest that an equally reliable barometer of progress is the attitude of the nation towards its paediatricians?

"Paediatrics as a specialized branch of medicine had no real existence before the middle of the last century. Its earlier history is only a small part of the main current of internal medicine", as Garrison wrote. It was an incidental, not the main part of the professional lives of doctors. As a specialty in its own right it probably evolved because infant feeding seems a subject apart, and infants themselves are so different from adults. After the sweat and blood and terror of delivering the mother, the obstetrician could hardly be expected to continue the same intense level of interest in the product or her labour and his. To the physician who looks after adults the infant, though doubtless a mammal, has sometimes seemed subhuman. The new specialty has inevitably grown and evolved still further.

Modern paediatrics focussed first on food. But, looking back now, nutrition seems to have been unnecessarily complicated and fussy; after all, most babies thrive on most milks, and babies have an internal timing and measuring device that tells them when and how much to feed—if only we do not put a spoke in the wheel. This sort of fussiness was probably necessary in the early exploratory efforts of the eo-paediatricians, and it applied not only to food but also, for example, to the stools. It is not so long since star-gazing as a pastime was rivalled in popularity by stool-gazing.

In the early decades of this century the physical aspects of illness absorbed nearly all the energies of paediatricians. At the time this was very proper, as it still is in the hungry countries of the world. But in this country the threat of acute physical disease is now receding. Only half a century ago, when some of us were born, six or seven infants and children died for each one that dies now. In England and Wales last year fewer than one hundred children died of tuberculosis. We are now approaching the hub of physical disorder in childhood. As a result, a very interesting new situation is developing.

To our predecessors it would seem a revolutionary concept that nearly all children are now expected to live. But it goes even further. Doctors, and especially paediatricians, have now to adapt themselves to the idea that patients are expected not only to live, but to enjoy living. This is coming about on the background of a steadily rising standard of living, a materialistic background; but there is a tendency to forget

that man does not live by bread alone. Going with a broader, not exclusively materialistic approach, is the implication of a mass attack on the non-physical aspects of healthy living—what we may describe in terms of psychology or social psychiatry, but from which morality and religion cannot be separated.

Can the problem be considered exclusively in medical terms, and will the answer be provided by drugs? I take leave to doubt it. What would happen to children given tranquillizers from birth onwards, to guard them against the emotional disorders of adult life? Though preventive psychiatry must offer almost inconceivable prospects for the human race, it is difficult to believe that in this field there will be equivalents to the insecticides or the antibiotics.

THE PAEDIATRIC SUB-SPECIES IN THIS COUNTRY

The consultant paediatric services in this country are based on hospitals. We hear rumours that paediatricians are "working themselves out of a job". We are told of children's wards that have more doctors than patients, take in lodgers to keep the cots and nurses occupied, or are being used for adult patients. The situation is worth thinking about. Let us examine one contributory factor alone, the National Health Service.

In this country before the N.H.S. era consultant paediatricians were a very small sub-species, their habitat only a few of the largest towns. Since 1948 their number has increased many times over, and they have now appeared in almost every part of these islands. In consequence, nearly every child who needs it can benefit from expert paediatric advice in or near his own home. Another consequence of the N.H.S. was decentralization. In some very large cities there may be empty paediatric wards—but is this so elsewhere? I affirm that very few paediatricians have time to twiddle their thumbs or to count napkins. Certainly they have too little time for the clinical research which is so much needed, or even to sit down and think.

We need many more facts, but here are a few. More children came to my out-patient clinics last year than ever before. Admissions to the paediatric beds in the hospitals where I attend are higher than they have ever been—though it must be added that a contributory factor is that children are not kept in hospital as long as they used to be. From the whole of the South West Region, with two-thirds of a million children under 15 years of age, I have figures that show a steady increase both of paediatric in-patients and out-patients until 1955, since when the level has remained steady. This region is probably representative of many others in that there are, in my view, too few paediatricians to deal with the many disorders which are now coming into their ambit. It seems clear that the paediatric services are held at their present level only because consultants are working at, and indeed beyond, their limit; if even a few more could be appointed the number of children efficiently dealt with would increase considerably.

A detailed investigation in Newcastle, published this year by Taylor and Davidson, tells a similar story. Between 1950 and 1957 there was little change in the admissions to children's hospitals in the Newcastle area. One point that will interest Management Committees is the demonstration from the Newcastle survey that if children are nursed in units *not* under paediatric supervision the length of their stay in hospital is appreciably increased.

It is true that doctors nowadays are rightly concerned to avoid admitting children to hospital, but in some respects this commendable reluctance may be pressed too far. If they do have to come into hospital we must ask, as Spence did, "What kind of hospital?". We should think not only of technical expertise but of many less definable factors. Neither keeping the child at home, nor ease of visiting if the child is admitted to hospital, can compensate for unnecessarily long illness, for avoidable physical or emotional sequelae, or for a dead child.

ENVIRONMENTAL FACTORS IN PAEDIATRIC EVOLUTION

Paediatrics abroad

Ireland has no snakes. Australia has kangaroos. Evolution on an island may proceed in a direction very different from that on large land masses, and we live on an island. In this country, for example, general practice has always been important, and we continue to believe in the patient-doctor relationship. But in some countries of Europe general practitioners are becoming as extinct as the dodo; they are being ousted by specialists, or they are succumbing to the modern medical disease—polyclinicosis. This evolutionary trend is not one that we should encourage here.

If we look further afield we see that in the U.S.A., for example, the evolutionary process differs from our own. Is it because of the extremely rapid growth of the population? In the U.S.A. there were 40 million children in 1940, and 57 million in 1957. Or is it because of the difficulties in maintaining a permanent patient-doctor relationship with so mobile a population? Or because of the widespread conviction that the new must be an improvement on the old? We have learned in other fields of knowledge not to ignore the Russians, and in paediatrics they must certainly be taken into account. Here I must draw on what I have read, for while my views on many countries in Europe and on North America are to some extent first-hand those on Russia are culled from others, a defect which I long to remedy. Perhaps the most impressive aspect of paediatrics in Russia is that emotional difficulties, psychosomatic disorders and neuroses seem so rare. Russian doctors use a Pavlovian rather than a Freudian approach to explore the workings of the mind, and education seems to be based on conditioning and the moulding effects of the community. But please observe that the child in Russia is the most important asset of the community, by edict of the Central Committee of the Communist Party. We need to know more about paediatrics not only in countries but in cultures other than our own.

Paediatrics in this country

Coming back to this island, there are many factors in our changing environment to which paediatricians must adapt. An obvious one is the increasing instruction of the public in medical matters by the press and the ubiquitous television. More fundamental factors are the uncertainty that is at present confusing educationalists; the watering-down of religious beliefs; the growing view that leisure, for women as for men, is a right and not a privilege; and the increasingly high standard of material living and of mechanization. All these indirectly affect medical practice. In medicine we have also the changing pattern of nursing and nurses; the trend away from the hospital to the home; and of course the National Health Service, with its many good features but its emphasis on disease rather than health, and its deplorable schism between general practice and hospital practice.

The Welfare State

Many of the factors that form the environment of paediatrics can be grouped under the heading of The Welfare State, with all that this implies both for good and for bad. In the Newsholme Lectures (1953) Moncrieff described how "The Welfare State has emerged by an evolutionary process in the sphere of social affairs but without sufficient education (or propaganda) to take the people along with all its implications", and in consequence "parents demand as a right to have everything done, and the next stage is almost a refusal to do anything themselves".

Let me select a few points from a paper by Richter published this year under the provocative title of "Rats, Man and the Welfare State". He quotes first some calculations about mechanization which came as a revelation to me. In the U.S.A. in 1939 the work performed by machines was equivalent to a hundred slaves per head of the population. In this country it was only fifty slaves per head. We are

obviously over-worked. Nevertheless we compare well with other countries, such as China with three or four slaves for each person. Like others before him Richter goes on to speculate about the incidence of incurable diseases and defective health (mental and physical) associated with civilization. To attempt an answer he compares men with rats—this has been done before—and wild with domesticated rats. With the transmission of mutations in the rodent welfare state, domesticity has permitted the survival of toothless rats, hairless rats, jaundiced, anaemic, blind, wobbly and waltzing rats.

The Welfare State should not however be blamed for developments that are attributable to civilization or to the progress of medical science. Nevertheless it is certainly true that in civilized countries, and particularly under a welfare state, many live who would otherwise die. In the domain of paediatrics we are responsible for the survival of many premature babies, rhesus babies, babies with congenital malformations, and others. Moreover, they may go on to reproduce their own defects in their offspring. Yet we must set against this the vast multitude of children who would have died, or would have limped through life, but have instead been given the opportunity of leading a full and healthy existence.

In the campaign against nature mankind is sheltering more and more behind the shield of medicine. As doctors we may feel flattered; as students and manipulators of evolution we may feel scared—but we should also be stimulated.

INTERNAL FACTORS

Since doctors are increasingly playing a part in modifying the evolutionary process we should study not only our environment but also ourselves.

In biological evolution migration is important; to some extent the environment is not merely accepted but selected. In paediatrics, similarly, some of the most active, as well as the most frustrated, among us tend to explore and to move on to promising new territories. They tend also to cross-breed, and in paediatrics I should like to encourage wholeheartedly the "hybrid vigour" that results from selective cross-breeding. In various sub-species of medicine there has been a tendency to in-breeding, with breeding centres at some well known institutes claiming to produce the only true thoroughbreds. Fortunately this tendency is becoming a thing of the past, for the thoroughbred is ill-suited to adapt to changing circumstances.

One point on which the moderns differ from Darwin is that his emphasis in evolution was entirely on competition; he neglected the opposing principle of co-operation in a species or sub-species, which we now know to be important. On the whole paediatricians co-operate rather than compete, especially since the inception of the National Health Service, with advantage to themselves, to the medical profession as a whole, and to their patients.

So much for some of the evolutionary factors that we can see at work; but many others that will affect ourselves or our patients are unpredictable. Thus in our Western civilization the onset of puberty is occurring earlier and earlier in the lives of children in successive generations; if this trend continues it may change not only medicine but civilization itself as we now know it.

THE FURTHER EVOLUTION OF PAEDIATRICS

In his *Descent of Man* Darwin discussed biological evolution in the past; Galton followed him by venturing into the future. I lay no claim to being a paediatric Galton, but it is stimulating to try to forecast, even though "we do but learn today what our better advanced judgements will unteach tomorrow".

In the near future attention in paediatrics is likely to be focussed more sharply on critical periods in the child's development. Puberty, for example, is now receiving long delayed attention; but, in the main, the focus is progressively shifting back in time. We are learning to read the child's palimpsest. We are exploring back beyond

infancy, beyond the critical first breath of life, to intra-uterine existence; and even further back, to microscopic chromosomes and mascroscopic family units.

The current trend to prevent disorder rather than to "cure" will be intensified. Accidents to children in the home and on the street are already being studied from this viewpoint. More and more disorders of infancy and of later life will be prevented as obstetricians become, in Professor Neale's stimulating term, "ante-natal paediatricians"; and as we pay increasing attention to parental and family wellbeing in all its dimensions. Now that so much progress has been made in the prevention of physical disorders, Public Health Departments are commendably turning their attention to mental health, a welcome transition which has been crudely summed up in the phrase "from drains to brains". The trend towards prevention of non-physical ailments is only now discernible, but will surely be strengthened.

What of specialization? We may remind ourselves that in biological evolution specialization is a necessity, though over-specialization may lead to extinction. Will specialists suffer the fate of the sabre-toothed tigers? You will recall that sabre-toothed tigers were believed to have died out through over-specialization; though, alas, it now seems that their extinction was not due to their teeth. The moral, however, is clear, and it is as well that paediatricians in general have evolved as consultants rather than specialists. They are unlikely to become extinct so long as they remain adaptable. No one person can any longer be expert in every aspect of paediatrics; but there will surely be a continuing need for paediatric consultants with a basic grounding in all aspects of growth and with an ability to mainain perspective.

I believe, however, that neither adaptability nor perspective can be achieved by living in ivory towers—though this is hardly an apt term for the primitive buildings in which many of us work. Paediatricians must surely go into the homes and the schools; they must study children in their natural environment. And, as some are already doing, they must try to break down the barriers between hospital doctors and family doctors and public health doctors—barriers of opportunity and of practice. We are all concerned with children. We are all, directly or indirectly, helping to mould what our American colleagues call the New Paediatrics, which embraces every aspect of childhood and is not restricted to "diseases".

What of the more distant future? There will, of course, be new diseases. I suspect that many of them will lie in the province of philosophy, where doctors have always found a congenial niche. Let me foreshadow only the substitution of deficiency diseases by "excess diseases". Having seen children of school-leaving age already needing a complete set of artificial teeth, and learning from my colleagues' pointed remarks that obesity in adults shortens life, I mention concentrated carbohydrates as one example of the excess diseases against which man may need to be protected.

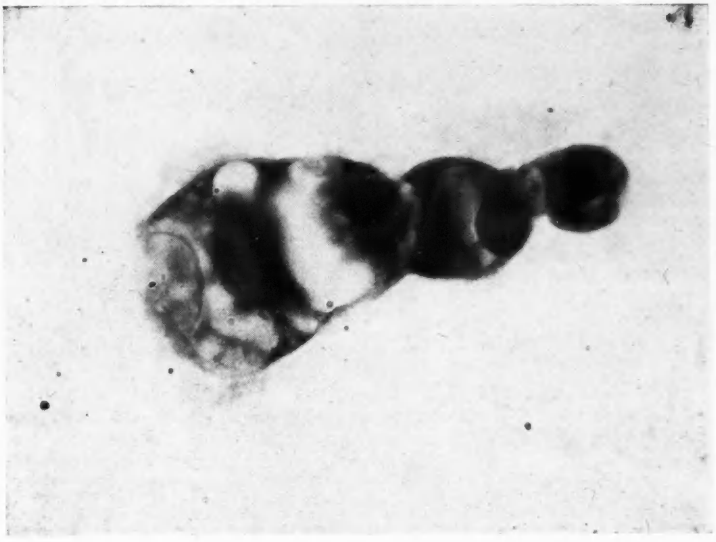
I fancy that one can foresee a Brave New World in which the Malthusian problem will no longer exist. There may come a time when none but the best potential parents will experience the desire to bear children. In predetermined numbers and sex, children will be born painlessly and atraumatically; and, following recent veterinary experiments, not singly but in litters. Few will suffer from congenital malformations, for these, like cancer, will have been virtually eliminated by the application of genetics and biochemistry. They will come into a world where there will be less need for surgeons—these carnivores will have to adapt themselves to a predominantly vegetarian diet. Nor will the genetically and biologically minded psychiatrists have so much to do, especially if stress, as I dare to hope, is controlled and used as the mental equivalent of muscle building. Our remote heirs will enjoy a long life before degenerative processes can no longer be profitably postponed. I foresee a time when there will be little work and much leisure for the doctor-philosophers who deal with adults—once paediatricians have learned to do their job properly.

In the centenary year of Darwin's *The Origin of Species* it has been stimulating for me, and I hope not uninteresting for you, to consider in evolutionary terms the

development of paediatrics, as one part of the profession to which we are all debtors. I do not conclude by suggesting that the Ministry of Health be replaced by a Ministry of Evolution—at least, not yet. But if we ponder on evolution in the past and the present we are the more likely to adapt successfully in a fast-changing world, and to direct our future rationally and purposefully.

My views have been deliberately optimistic, as befits a doctor of children who is inevitably and pleasantly influenced by his patients. You were not meant to agree with all my forecasts; but you will agree that while children continue to be born paediatrics will continue to be practised, and that paediatrics will always be worthwhile—for, "As the twig is bent so the tree will grow".

PLATE XV



Smear from C.S.F. deposit, showing collection of malignant cells.
(X1100)

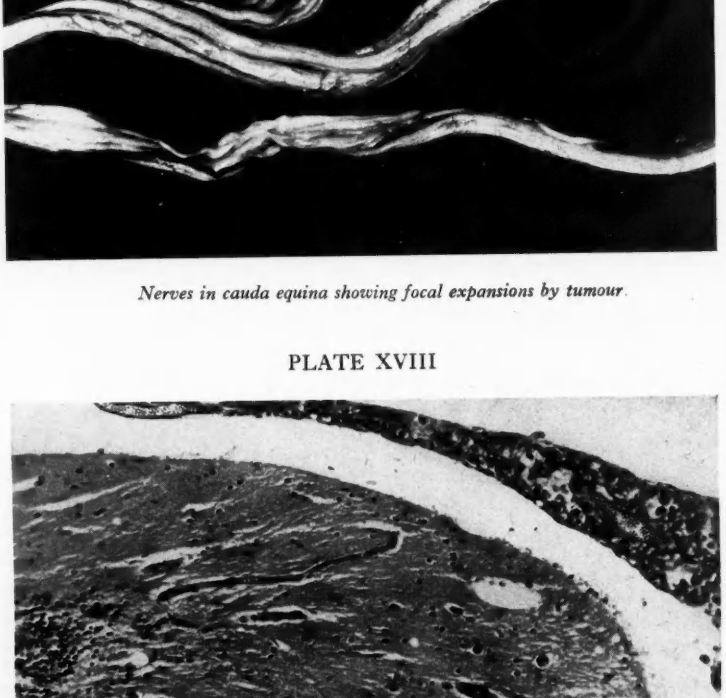
PLATE XVI

Uniform enlargement of right optic nerve through infiltration by tumour.

PLATE XVII

Nerves in cauda equina showing focal expansions by tumour.

PLATE XVIII



Photomicrograph of section showing infiltration of cerebellum and meninges by poorly differentiated adenocarcinoma.

(x60)

A CASE OF MENINGEAL CARCINOMATOSIS

A Clinical Pathological Conference of the University of Bristol Medical School
(P.M. 6388)

CHAIRMAN: DR. O. C. LLOYD

(Though discussed at a Clinical Pathological Conference there was, unfortunately, no record of the proceedings kept. The case is therefore now presented as a report.)

Dr. C. F. Allenby, deputizing for Dr. J. E. Cates, presented the clinical picture: The patient, a man of 38, worked as a cable layer. In September, 1959, he was hit in the chest by a sledge-hammer and dated his illness from this injury. A week later he was admitted to Ham Green Hospital with pneumonia. Response to penicillin, and later to streptomycin, was slow and X-ray of his chest revealed a cavity in his right lung. He discharged himself against advice and did not attend for further X-rays. In October, 1959, when turning in bed he felt a sudden pain in his back which later spread down both legs. He was seen in the Orthopaedic Department and then referred to Dr. J. E. Cates. The only other feature in his history was that in 1957 he was off work for 8 months with pain in his back after an injury when lifting sacks at work.

In the Out-Patient Clinic he was seen to be thin and ill. There was clubbing of his fingers. There was 1 in. wasting of the right thigh with impairment of sensation over the right leg and depressed right knee jerk.

He was admitted for further investigation a few days later and developed in this short time fresh neurological signs and symptoms. His right eye had become blind; the left third cranial nerve was paralyzed. There was a slight left facial palsy; besides the lower motor neurone signs in the right leg there were now signs of right pyramidal damage. The patient had periods of mental confusion.

Radiological examination revealed a fibrotic lesion in the right upper zone of the lung with cavitation and shift to the right of the upper mediastium. Degenerative changes were noted in the fifth lumbar vertebra and sacrum, possibly osteophytes. Carotid angiograms were normal.

Sputum and gastric washings showed no acid-alcohol-fast bacilli. W.R. and Kahn negative. Lumbar puncture showed a clear fluid, not under pressure, with slow rise and fall on jugular vein compression.

Dr. A. B. Weber described the C.S.F. findings: The sugar was reduced to 25 mgm per cent, protein 76 mgm per cent with increased globulin, and a pleocytosis of 27 c/mm consisting of 63 per cent lymphocytes and 37 per cent "large mononuclears" which were considered to be malignant cells (Plate XV).

Dr. Allenby continued: Bronchoscopy was performed, but revealed no evidence of carcinoma. The patient died about 4 months after the onset of symptoms. During life several diagnoses were considered; the most likely seemed to be meningeal carcinomatosis, the primary source of which had not been localized.

Dr. N. G. Sanerkin then described the necropsy: The body was that of a well-developed rather wasted adult male, with early finger clubbing. The right pleural cavity was obliterated supero-posteriorly by dense fibrous adhesions, and there was a right basal serofibrinous pleurisy. A left tonsillar abscess was found, which proved to be streptococcal. The right lung showed an irregular area of collapse-consolidation in the posterior part of the upper lobe, with ill-defined areas of induration, bearing numerous necrotic cavities which did not contain pus. There was surrounding fibrosis and emphysematous bullae, with a large bullous sac (10 cm in diameter) at the apex. The right lower lobe showed well-developed bronchopneumonia with pleurisy.

The left lung was free from tumour, but showed generalized emphysema with apical fibrosis, patchy basal collopse, some oedema and bronchiolitis.

A few of the right hilar lymph nodes were enlarged and infiltrated by tumour. The tracheobronchial, paratracheal, mediastinal, axillary, para-aortic, paragastric, mesenteric and iliac lymph nodes were infiltrated by tumour. Extension of tumour from the paratracheal nodes had involved the right recurrent laryngeal nerve. A large lymph node below the carina showed early tumour infiltration but no fixation, much of the enlargement being due to reactive hyperplasia.

Small tumour deposits were found in both adrenals, both kidneys, left tonsil, spleen and rectum; but none were present in the liver or pancreas. Multiple tumour deposits were found in the bones, especially skull and vertebrae.

The most remarkable findings were in the meninges, brain, and cranial and spinal nerves. The dura was studded with small plaques of tumour, mostly in the falx cerebri and tentorium cerebelli. The brain showed numerous tumour deposits (the largest 2 cm in diameter), mainly cortical in distribution, but with a few nodules in and around the basal ganglia; they were mostly solid, greyish-white, with areas of central necrosis, but a few were clearly mucoid and translucent. Similar nodules were found in the cerebellum. The right optic nerve was considerably and uniformly enlarged by tumour (Plate XVI). Similar enlargement was noted in the left oculomotor nerve. Small tumour deposits were present in the cauda equina (Plate XVII), and higher up in and around the spinal nerves, but no deposits were found in the spinal cord itself. There was no intervertebral disc herniation.

Histological examination showed a rather poorly differentiated adenocarcinoma of the lung, growing in parts in loose collections of spheroidal cells, in others showing tubular and acinar differentiation, with occasional production of mucin, and a distinct tendency to alveolar spread. The cerebral metastases showed much more obvious mucoid change. Mengineal infiltration was patchy, and was especially noted around the cerebellum (Plate XVIII) and spinal cord. The right optic nerve, and the other enlarged nerves, were diffusely infiltrated by tumour. A section from the left retina also showed deposits of tumour.

Necropsy diagnosis: Mucoid adenocarcinoma of lung, with multiple metastases and meningeal carcinomatosis. Apical pulmonary fibrosis; bullous emphysema. Streptococcal tonsillar abscess. Terminal bronchopneumonia.

This case provided a fairly typical clinical example of "meningeal carcinomatosis" with typical C.S.F. findings, including a low glucose level and the presence of malignant cells; indeed the discovery of the latter was the first indication of a malignant process in the patient.

McMenemy and Cummings (1959) state that tumour cells are frequently found in the C.S.F. in meningeal carcinomatosis, especially when the cauda equina is involved. They stress that a low glucose level is highly suggestive of carcinomatous meningitis, and should stimulate search for tumour cells.

Jacobs and Richland (1951) and Fischer-Williams, Bosanquet and Daniel (1955) provide case reports and review the literature. Their criteria for the diagnosis of meningeal carcinomatosis are (i) the presence of metastatic carcinoma cells in the subarachnoid space and (ii) the absence of gross nodule formation in the central nervous system. They consequently exclude all those cases in which gross metastatic nodules are present in the central nervous sysyem. They emphasize that the condition forms a distinct clinical and pathological entity. Clinically, the prominent features include headache, varying degrees of dementia, constipation, cranial nerve palsies, especially blindness. The majority of cases are secondary to adenocarcinomas, usually of the gastro-intestinal tract or lung. Fischer-Williams *et al.* (1955) state that of fifty bronchial carcinomas with intracranial metastases only three were adenocarcinomas, and all three had produced diffuse leptomeningeal spread (one of them with cerebral deposits as well).

Heathfield and Williams (1956) record two cases, with fairly typical clinical histories; one of their cases, however, like the present case, had tumour nodules in the brain.

From the clinical aspect, the present case was certainly an example of "meningeal carcinomatosis". Pathologically, too, it showed leptomeningeal dissemination, with infiltration of cranial and spinal nerves. Fischer-Williams *et al.* would exclude this case, since tumour nodules were present in the brain. Nevertheless, it is pertinent to suggest that the presence or absence of such nodules may be largely immaterial, the important factor being the behaviour of a given tumour in the leptomeninges and subarachnoid space, no matter whether it gets there exclusively or in conjunction with cerebral metastases.

REFERENCES

Jacobs and Richland (1951). *Bull. Los Angeles Neurol. Soc.*, **16**, 335.
Fischer-Williams, Bosanquet and Daniel (1955). *Brain*, **78**, 42.
Heathfield and Williams (1956). B.M.J., **i**, 328.
McMenemy and Cummings (1959). *J. Clin. Path.*, **12**, 400.

News from Societies

PROGRAMMES FOR 1960–61 SESSION

UNIVERSITY OF BRISTOL

POSTGRADUATE COURSES

The following course is being arranged:

Sunday morning Lecture-demonstrations, from 24th October to 11th December, 1960. Details may be obtained from the Department of Postgraduate Medical Studies.

BATH CLINICAL SOCIETY

Secretary: Dr. J. R. Bolton, 61 Englishcombe Lane, Bath

14th Oct.: **Clinical Meeting** at St. Martin's Hospital, Bath.
11th Nov.: Dr. R. Bishton, Dr. D. W. Pugh, Mr. Stuart-Black Kelly: **Symposium on Diabetes Mellitus**
9th Dec.: C. P. Sames, Esq., M.S., F.R.C.S., **"Peripatetic Proctology"**
13th Jan.: Dr. J. M. Drew, **"From Bed to Worse"**; Dr. J. Beviss, **"From Dizzy Heights"**
10th Feb.: **Clinical Meeting**
10th Mar.: Dr. Richard Asher, M.D., F.R.C.P., **"Hypnosis in General Medicine"**
14th Apr.: Bryce Blair, Esq., F.R.C.S., F.R.O.G., **"Variations on a Theme"**
12th May: **Annual General Meeting**
All Meetings will be held at the Royal United Hospital, Bath, unless otherwise stated.

B.M.A. (CORNWALL DIVISION)

Hon. Secretary: Dr. Eric Townsend, Fieldways, Tregenna Lane, Camborne

24th Nov.: **Annual Dinner and Dance,** Hotel Bristol, Newquay.
24th Mar.: Professor M. L. Rosenheim, **B.M.A. Clinical Lecture,** Royal Infirmary, Truro, 8.30 p.m.

B.M.A. (GLOUCESTERSHIRE BRANCH)

Hon. Secretary: Dr. H. G. Scott-Kerr, 29 Leckhampton Road, Cheltenham

13th Oct.: Mr. J. D. J. Freeman. **Presidential Address: "A Naval Opthalmologist in Ceylon",** and a film, colour and sound, **"Land of the Buddha"** Gloucester.
10th Nov.: **Representatives' Report.** Financial Statement. Film. Cheltenham.
8th Dec.: Guest Speaker: Mr Brian Inglis, Editor of *The Spectator*. Combined Meeting with the Press. Gloucester.
12th Jan.: Dr. P. G. Mann. Director, Public Health Laboratory, Bath. Paper: **"Chemotherapy of Acute Infections"** Cheltenham.
9th Feb.: Dr. D. Lindsay Walker, **"Some Psychiatric Concepts where Emphasis is misplaced".** Gloucester.
9th Mar.: **Clinical Meeting.** Cheltenham.
13th Apr.: P. D. Trevor-Roper, Esq., M.D., D.O.M.S., F.R.C.S. (Doctors' Ladies to be invited). B.M.A. Lecturer. Address: **"Influence of Eye Disease on the Artist",** illustrated with slides. Gloucester.
11th May: Mr. R. J. Hart. **Annual Meeting and Paper: "Problems in the Early Diagnosis of Bone Disease".**
8th June: Dr. Richard Sydney Allison, Senior Physician, Royal Victoria Hospital, Belfast. **President's Guest.** Gloucester.
Unless otherwise stated the meetings will be held at 6.15 p.m. The place of the meetings will be stated in the circular notices.

B.M.A. (SOUTH-WESTERN BRANCH)

Hon. Secretary: Dr. F. E. Graham-Bonnalie, 37 The Strand, Topsham, Nr. Exeter

17th Nov.: **Combined Meeting** with the Exeter and South Devon Medico-Chirurgical Society.
3rd Dec.: **Autumn Clinical Meeting** at Plymouth.

BRISTOL NORTH AND WEST GROUP OF GENERAL MEDICAL PRACTITIONERS

Hon. Sec.: Dr. C. Jean Fraser, 20 Dragon's Well Road, Henbury, Bristol

Meetings on the second Tuesday of each month during winter. Programme to be arranged.

PLYMOUTH MEDICAL SOCIETY

Meetings at 8.30 p.m.

Secretaries: Dr. Bernard Peck, 5 Lockington Avenue, Hartley, Plymouth and Mr. Michael Reilly, Cresswell, Hartley Avenue, Plymouth.

14th Oct.: Dr. J. W. Landells, M.R.C.P., **"The Dangers of Medical Treatment"**, North Friary House.
28th Oct.: **Clinical Evening** (Cases from 8 p.m.), Freedom Fields Hospital.
4th Nov.: G. L. Alexander, Esq., F.R.C.S., **"The Danger Signs in Cases of Head Injury"**, North Friary House.
18th Nov.: Dr. Richard Asher, M.D., F.R.C.P., **"See How They Come"**, Joint Meeting with Plymouth Division, B.M.A., North Friary House.
23rd Nov.: **Annual Dinner and Dance,** Duke of Cornwall Hotel.
9th Dec.: **"Mutual Problems"**, Joint Discussion Meeting with Plymouth Section, British Dental Association, North Friary House.
20th Jan.: Prof. J. Chassar Moir, D.M., F.R.C.S., F.R.C.O.G., **"Some English Queens and their Confinements"**, North Friary House.
3rd Feb.: Prof. J. H. Burn, M.D., F.R.S., **"The Action of Reserpine in Peripheral Vascular Disease"**, North Friary House.
14th Feb.: **Clinical Evening.** (Cases from 8 p.m.), Royal Naval Hospital.
3rd Mar.: **Short Papers** by: Dr. G. B. Carter, Dr. T. L. Chester Williams, Mr. I. Sutherland-Jones and Dr. B. J. Peck, North Friary House.
4th Apr.: **Clinical Evening** (Cases from 8 p.m.), Freedom Fields Hospital.
3rd May: Visit to Ellbridge Experimental Horticultural Station. (Members' Ladies also invited), Nr. Saltash.
8th May: **Annual General Meeting,** North Friary House.

COSSHAM MEDICAL SOCIETY

Secretary: Dr. K. W. Moulding, 235 Lodge Causeway, Bristol

4th Oct.: Mrs. Z. M. U. Eastes, M.R.C.S., L.R.C.P., **Presidential Address.**
1st Nov.: H. Leather, Esq., M.D., M.R.C.P., **"Medicine in Africa".**
6th Dec.: H. L. Shepherd, Esq., M.B., CH.M., F.R.O.G., **"Maternal Mortality".**
17th Dec.: Cheese and Wine Party at Marshfield.
3rd Jan.: S. F. Marwood, Esq., M.D., M.R.C.P., **"Treatment in Diabetes—a review".**
7th Feb.: A. C. Hunt, Esq., M.D., B.S., **"Unnatural Deaths".**
7th Mar.: Miss B. D. Corner, M.D., F.R.C.P., **"Early Arrivals, what are the later results?".**
4th Apr.: **Annual General Meeting.**

ROYAL DEVON AND EXETER HOSPITAL POSTGRADUATE PROGRAMME

Secretary: Mr. H. Dendy Moore, 4 Magdalen Road, Exeter

The Exeter Postgraduate Meetings will take place on Tuesdays at 8.30 p.m. from 11th October to 6th December, 1960.

SOCIETY OF MEDICAL OFFICERS OF HEALTH WEST OF ENGLAND BRANCH

Secretary: Dr. R. H. G. H. Denham, Council Offices, 8 Cleveland Place, East, Bath.

The Society is divided into two sections, Northern and Southern. Each section holds four meetings a year, one of which being a joint meeting of both sections.
1st Oct.: E. D. Irvine, Esq., M.D., D.P.H., M.O.H., Exeter. **Presidential Address.** (Taunton).
7th Jan.: At Bristol. (details later).
1st Apr.: **Joint Meeting** of Northern and Southern Sections. (Details later).
June. At Bath. (Details later).

WESSEX RAHERE CLUB

The autumn dinner of the above club will take place on 29th October, 1960, at the Grand Spa Hotel, Clifton, Bristol, under the Chairmanship of Dr. Russell Grant of Winchester. It is hoped the Guest of Honour will be Dr. Heber Langston. Further details will be circulated or can be obtained by any Barts. graduates who are not already members from the Hon. Secretary, Mr. A. Daunt Bateman, F.R.C.S., 11 The Circus, Bath.

Appointments

SOUTH WESTERN REGIONAL HOSPITAL BOARD

March 1960 to June 1960

BRISTOL

Name	*Appointment*	*Formerly*
PHILPOTT, B., M.B., B.S. (LOND.), D.A.	Registrar in Anaesthetics, Frenchay Hospital.	Anaesthetic Registrar-United Bristol Hospitals.
MCCLELLAND, H. A., M.B., B.S. (DUR'M). D.O.R.C.O.G., D.C.H.	Medical Registrar, Southmead Hospital.	Medical Registrar, Cheltenham General Hospital.
BROWSE, N. L. M.B., B.S. (LOND.), F.R.C.S. (Eng.).	Surgical Registrar, Southmead, Hospital.	Research Assistant to Professor R. Milnes Walker.
BURGESS, T. P., M.R.C.S., L.R.C.P.	Registrar in Psychiatry, Bristol Mental Group.	S.H.O. in Psychiatry, Barrow Hospital.
FLOOD, R. A., M.B., CH.B. (ST. ANDREWS)	Registrar in Psychiatry, Bristol Mental Group.	Registrar in Psychiatry, Bristol Mental Group.
GYAW, C. P., M.B., B.S. (RANGOON), D.A. (LOND.).	Anaesthetic Registrar, Southmead Hospital.	Locum Anaesthetic Registrar, Southmead Hospital.
MATHEWSON, HELEN S., M.B., CH.B. (ST. ANDREWS), D.P.M.	Registrar in Child Psychiatry & Mental Deficiency, Horfham-Brentry Group.	Registrar in Psychiatry, Prestwich Hosp., Nr. Manchester

BATH

ZAIDI, S. K. H., M.B., B.S.	Registrar in Anaesthetics to the Bath Group of Hospitals.	Resident Anaesthetist (S.H.O.) Epsom District Hospital.
CRAWFORD, J. W., M.B., CH.B. (GLAS.) D.O.R.C.O.G.	Registrar in Obst. & Gynae., Bath Group of Hospitals.	Registrar in Obstetrics, Forth Park Maternity Hospital.
DUCAT, E. F., M.B., CH.B. (ABERDEEN)	Clinical Assistant in Paediatrics, Royal United Hospital.	In general practice in Batheaston. Also present holder of Clinical Assistant post.
CHANDRASEKARAN, M. S. I. B.SC., M.B., B.S. (MADRAS), D.L.O. (LOND.)	Registrar in E.N.T. Surgery to the Bath Group of Hospitals.	E.N.T. Registrar, Bath Group of Hospitals.
HEAP, L. D., M.R.C.S., L.R.C.P.	Registrar in Pathology to Bath Group of Hospitals.	Resident Clinical Pathologist (S.H.O.), St. George's Hosp., London, S.W.1.
BURROWES, W. L., M.D., M.R.C.P	Clinical Assistant in General Medicine to the Bath Group of Hospitals, for one year.	Clinical Assistant in General Medicine to the Bath Group of Hospitals, and in general practice.
PINCHING, J., B.M., B.CH., M.R.C.P.	Clinical Assistant to Royal United Hospital, Bath.	Clinical Assistant to Royal United Hospital, Bath, and in general practice.
ELLISON, D. J., M.B., CH.B., M.R.C.P.	Clinical Assistant to Royal United Hospital, Bath, for one year.	Clinical Assistant to Royal United Hospital, Bath, and in general practice.
RONN, H. H., M.B., B.S., M.R.C.P.	Clinical Assistant to Royal United Hospital, Bath, for one year.	In general practice in Westbury, Wilts.
DUNBAR, P. G., M.B., B.S. (Lond.), D.A., D.OBST., R.C.O.G.	G.P. Anaesthetist, Devizes.	In general practice, Devizes.

NORTH GLOUCESTERSHIRE

Name	*Appointment*	*Formerly*
SOLTAU, D. H. K., M.A., M.B., B.CHIR.(CANTAB)., F.R.C.S.(ENG.), M.R.C.O.G.	Consultant Obstetrician and Gynaecologist to the North Gloucestershire Clinical Area.	Senior Registrar in Obstetrics and Gynaecology, St. George's Hospital and Southampton Group of Hospitals.
THOMSON D. S., M.B., B.S. (DUR'M.) D.O.M.S., F.R.C.S. (ED.).	Consultant Ophthalmic Surgeon to North Gloucestershire Clinical Area.	Senior Registrar, Oxford Eye Hospital.
DAVEY, R B., M.B., B.S. (SYDNEY)	Surgical Registrar, Gloucestershire Royal Hospital.	
MULLALLY, SHEILA, M.B., B.S., D.A.	Anaesthetic Sessions, Standish/ Stroud.	In general practice combined with anaesthetic sessions at Cheltenham.
PARKER, SHEILA M., M.B., CH.B., (BIRMINGHAM), D.A., F.F.A., R.C.S.	Anaesthetic Sessions, Standish/ Stroud.	In general practice in Stroud, Gloucestershire.
SHEPHARD, G. D. H., M.A., M.B., B.CHIR. (CANTAB.), D.OBST.R.C.O.G.	G.P. Anaesthetist, Tewkesbury Hospital.	In general practice in Tewkesbury.
GOMPERTZ, R. M. H. M.B., B.S. (Lond.), D.OBST.R.C.O.G., D.C.H.	Clinical Assistant in Paediatrics, Cheltenham Gen. and Maternity Hospitals.	In general practice in Cheltenham.

DEVON AND EXETER

PRYER, D. L., M.B., B.S. (LOND.), F.F.A.R.C.S.	Consultant Anaesthetist to the Torbay Area.	Senior Registrar in Anaesthetics to the Oxford Regional Hospital Board.
GIBBS, D. F., CH.B. (ED.). M.R.C.P. (ED.)	Assistant Geriatrician (S.H.M.O.) to the Devon & Exeter Clinical Area.	Registrar, Lansdowne Hospital, Cardiff.
JEFFERIES, GILLIAN A., M.B., B.S. (LOND.), D.A.	Registrar in Anaesthetics, Royal Devon & Exeter Hospital.	S.H.O. in Anaesthetics, St. Mary's Hospital, Portsmouth.
SOUTHWOOD, W. F. W. M.B., B.CH. (CANTAB.), M.A.(CANTAB.), F.R.C.S. (ENG.), M.CHIR. (CANTAB.)	Senior Surgical Registrar (Joint appointment with United Bristol Hospitals).	Research Asst., St. Mark's Hospital, London.
COOPER, R. A., M.B., B.S.	Temporary G.P. Anaesthetist, Bideford Hospital.	General Practitioner, Bideford.

PLYMOUTH

GORDON, D. T., M.B., CH.B., D.P.H. (ABERDEEN)	Senior Hospital Medical Officer in Infectious Diseases at the Scott Isolation Hospital, Plymouth.	Junior Hospital Medical Officer, Ham Green Hospital, Pill, Nr. Bristol.
CAM, J. F., M.B., B.S. (LOND.).	Registrar in Anaesthetics, South Devon & East Cornwall Hospital, Plymouth.	J.H.M.O., South Devon & East Cornwall Hospital.
COUTTS, J. P., B.SC. (N.Z.), M.B., CH.B.(N.Z.), F.R.C.S. (ENG.)	Surgical Registrar, South Devon & East Cornwall Hospital, Plymouth.	Locum Neurosurgical Registrar, Whittington Hospital, London.
MOSS, M. C., M.B., B.S., (ANDHRA) D.P.M. (CONJOINT)	Senior Registrar in Psychiatry, Moorhaven Hospital.	Psychiatric Registrar, Deva Hospital, Chester.

CORNWALL

Name	*Appointment*	*Formerly*
ANDERSON, I. F., B.SC. (LOND.). M.R.C.S., L.R.C.P.	Registrar in Obstetrics and Gynaecology, Camborne-Redruth Hospital.	Locum Registrar in Obstetrics and Gynaecology, Camborne-Redruth Hospital.
BAIN, C. W. C., B.M., B.CH. (OXFORD), M.R.C.P., D.M., F.R.C.P.	Clinical Assistant in General Medicine, Royal Cornwall Infirmary.	Retired September, 1958, as Consultant Physician.